# Bronchial artery embolization in patients with life-threatening massive hemoptysis: comparison of the efficacy and safety of particulate embolizing agents and n-2-butyl-cyanoacrylate

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**Abstract.** – **OBJECTIVE:** Comparing the efficacy and safety of particulate [microspheres/polyvinyl alcohol (PVA)] and non-particulate [n-butyl-2-cyanoacrylate (NBCA)] agents used as the embolic agents for bronchial artery embolization (BAE) intervention in patients experiencing massive hemoptysis.

**PATIENTS AND METHODS:** A total of 58 individuals (47 male, 11 female, standard deviation =  $53.9 \pm 14.8$ , age range = 18-84) were recruited for a retrospective study in a single unit. Thirty (51.7%) of the patients underwent BAE intervention with NBCA, and 28 (48.3%) underwent the same procedure with a particulate embolizing agent (microspheres/PVA). The demographic distribution of the patients, the etiological factors, the technical and clinical success rates, and complications were documented, with the two groups subsequently compared.

**RESULTS:** The technical and clinical success rates following the procedure were 100% for both groups. The average follow-up duration was 34 months in the NBCA group and 33.5 months in the particulate embolizing agent group. In comparison, the rate of recurrent hemoptysis was 3.3% in the former and 17.9% in the latter, with the presence of recurrent hemoptysis not statistically different between the two groups (p = 0.097). Major complications and procedural death did not occur in either of the samples.

CONCLUSIONS: The use of NBCA in BAE presents a safe and effective method. The combination of NBCA and particulate embolizing agents (PVA/microspheres) achieved equal technical and clinical success and significantly increased the hemoptysis-free survival rates in terms of life-threatening hemoptysis. Main Points: (1) In managing massive hemoptysis, using NBCA is a safe and effective method similar to using particulate embolizing agents. (2) Although not statistically significant, recurrent

hemoptysis is observed less frequently in the NBCA group. (3) Technique and clinical success were relatively high and similar in the groups where NBCA and particulate embolizing agents were used.

Key Words:

Bronchial artery, Embolization, Hemoptysis.

#### Introduction

Massive hemoptysis is defined as 100- to 1,000-mL bleeding from the respiratory tract for periods over 24 h (300-600 mL is the standard threshold)<sup>1,2</sup> and presents a medical emergency that is challenging to diagnose and treat, has a high mortality rate, and has several causes. In most cases, the source of massive hemoptysis is the bronchial arteries or the non-bronchial systemic collateral vessels.

The advent of advanced medical imaging, fiberoptic technology, and interventional radiology over the past 50 years has improved patient outcomes and reduced mortality rates. The traditional methods emphasize emergency surgery and are largely conservative, while the bronchial artery embolization (BAE) procedure has emerged as an effective alternative method with minimal invasion<sup>3</sup>. Meanwhile, the bronchial artery embolization (BAE) procedure was introduced by Remy et al<sup>4</sup> in 1973<sup>5</sup>. This procedure is regarded as a highly effective and minimally invasive alternative to surgery for massive and recurrent hemoptysis<sup>6</sup>. However, since the procedure does not address the underlying disease, hemoptysis generally recurs and requires frequent embolization<sup>7</sup>.

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The recent advances in embolic materials and embolization techniques have also facilitated specific technical improvements<sup>7,8</sup>. There is currently no agreement on which type of embolic material is considered to be the most effective. At the same time, absorbable gelatin sponge particles or polyvinyl alcohol (PVA) particles remain the materials most commonly used as embolic agents, largely because they are easy to use, are controllable in terms of embolic size, and are comparatively affordable<sup>7</sup>. In addition, various types of coils and microspheres have also been used in the BAE procedure1. Recently, n-butyl-2-cyanoacrylate (NBCA) has received a great deal of attention as an embolic agent for controlling bleeding in various organs<sup>7</sup>. The widespread use of liquid embolic agents, especially in terms of treating cerebral and spinal arterial malformations, has increased the overall efficacy in controlling the behavior of such materials<sup>5</sup>. In fact, NBCA has an array of advantages, including providing a more reliable embolization, the rapid occlusion of the target vessels, and the availability of various adjustment options, with iodized oil used to control the polymerization time and embolization safety of the target vessels<sup>7,9</sup>. However, despite the advantages, the use of NBCA in BAE procedures has tended to be avoided due to concerns over the high risk of severe complications, such as tissue necrosis and off-target embolization from uncontrolled reflux<sup>7</sup>.

Considering the aforementioned, this paper aimed to compare the efficacy and safety of particulate (microspheres/PVA) and non-particulate (NBCA) agents used as embolic agents in the BAE procedures for patients referred after experiencing massive hemoptysis.

#### **Patients and Methods**

# **Patients**

This study was conducted as a retrospective study pertaining to a single center. Each patient signed a comprehensive written informed consent form prior to the procedure, and approval was obtained from the relevant ethics committee [Baskent University Institutional Review Board (Project No.: KA20/349)]. The study relates to the documentation and medical records from January 2011 to July 2022, held in the computerized environment registered at our hospital for patients who underwent a BAE procedure due to massive hemoptysis. Our interventional radiology department treated sixty-three patients who underwent

BAE intervention for life-threatening massive hemoptysis. Five of these patients were excluded from the study due to a lack of a follow-up and insufficient documentation, meaning a total of 58 individuals (47 male, 11 female, standard deviation =  $53.9 \pm 14.8$ , age range = 18-84) were recruited for the study.

All the patients had experienced massive hemoptysis, with their average hemoptysis volume in a 24-hour period 489.1  $\pm$  197.9 mL (standard deviation, median 450 mL/min-max 300-1,000 mL). Thirty (51.7%) of these patients underwent BAE intervention with NBCA, and 28 (48.3%) underwent the same procedure with a particulate embolizing agent. The attendant bronchoscopy and contrast-enhanced computed tomography (CT) images were examined to detect any lung pathologies, the underlying causes, and the hemoptysis extent before the procedure to determine the possible bleeding focus and identify the vessels causing the bleeding. While a contrast-enhanced thorax CT examination is a routine process in our center, a bronchoscopy-centered approach is preferred in some cases (e.g., in unstable patients, when the active bleeding requires endobronchial therapy or when the bleeding localization cannot be detected via CT scanning due to bilateral lung pathologies<sup>10</sup>. Eighteen patients underwent a bronchoscopy test, with the bleeding focus identified in 15 (83%) cases, while the bleeding focus was detected in all 58 (100%) patients who underwent a contrast-enhanced CT examination. Contrast-enhanced CT has also been used to exclude collaterals from the internal thoracic, subclavian, or intercostal arteries supplying the bleeding site.

The relevant primary data (demographic, etiology, and hemoptysis details) were collected using an electronic medical record system, image archiving, and a number of communication systems (nucleus v9.29.67 MONAD software and consultancy, Ankara; Turkey). The prevalence of lung disease was categorized as 0-5 according to the number of lung lobes with disease involvement revealed *via* CT. The image interpretation was performed in terms of the consensus decision of three authors who did not know the embolic effect and did not see the results (M.M., I.K., and C.A., with 10, 5, and 20 years of experience in BAE, respectively).

# The Bronchial Artery Embolization Procedure

All angiographic procedures were performed by an interventional radiologist with at least five years of experience, with BAE performed during active bleeding or after the bleeding had stopped. After securing femoral arterial access with a 5-F vascular sheath, aortography covering the thoracic and upper abdominal aorta was performed using a 5-F pigtail catheter with the tip in the ascending aorta at a flow rate of 15 mL/s for 2 s and a frame rate of 3 frames/s in the anteroposterior position. Selective angiograms of the bronchial and non-bronchial systemic collateral arteries detected via contrast-enhanced CT and aortography were obtained using 5-F angiography catheters, with 5-F Sim 2, Sim 1, and USL 2 (Cordis Corporation, FL, USA) catheters used to identify the bronchial artery patency. Here, abnormal congestion, parenchymal hypervascularity, bronchopulmonary shunt, and the extravasation of the contrast medium following bronchial angiography were regarded as pathological indicators<sup>7,11</sup>. Once the bleeding was detected, a microcatheter was inserted coaxially into the angiographic catheter and extended along the pathological artery to the most distal segment near the vascular blush.

Meanwhile, the choice between the use of NBCA or particulate embolic agents was not regulated but was randomized based on the preference of the interventional radiologist. Both methods were used routinely throughout the study period without a transition period. All pathologically evaluated bronchial and non-bronchial systemic collateral arteries were closed.

The NBCA (Histoacryl, B. Braun, Melsungen, Germany) was mixed with a lubricated iodinated contrast agent (Lipiodol Ultra Fluide; Guerbet, Roissy, France) at 12.5-25% for use in the NBCA group. The mixture was then transferred to a 2-ml Luer lock syringe after the microcatheter was flushed with a 5% dextrose solution to prevent the fluids from sticking and to avoid any possible catheter clogging during NBCA injection. The mixture was carefully injected under fluoroscopy, with the distal end of the microcatheter ideally kept in a straight line to control the NBCA injection. The injection was continued with pulses after the first drop of NBCA was observed to emerge out of the tip of the microcatheter. Any reflux covering the distal end of the microcatheter was carefully monitored. The mixture's ratio, volume, and injection speed were varied according to the embolization size and flow, and the microcatheter was quickly removed after injection to prevent the catheter tip from sticking to the vessel wall.

Microspheres or PVA (Embozenes, 300-700 μm, CeloNova Biosciences, Inc., Peachtree City,

GA, USA; Bead Block Embolic Bead, 300-700 μm, Biocompatibles, Inc., UK; Hydropearl Compressible Microsphere, 300-700 μm, Terumo, Inc., USA; Contour PVA Embolization Particles, 250-355 μm or 355-500 μm, Boston Scientific, Inc., USA) particles larger than 250 μm were used to prevent bronchial necrosis<sup>11,12</sup>. The mixture was injected into a 20-mL reservoir syringe *via* a 3-way stopcock and 1-mL injectors following dilution with 3 ccs of contrast and normal saline. The injection was continued with small pulses until reflux or stagnation occurred from the embolized arterial branch while carefully monitoring the fluoroscopic guidance.

Aortography was performed after the NBCAor PVA/microsphere-based embolization had been completed to confirm the presence/absence of other hemoptysic arteries.

# Technical and Clinical Success Assessment and Follow-up

Complete embolization of the bronchial and non-bronchial systemic collaterals targeted by the embolization was considered to be a technical success<sup>13</sup>, while clinical success was expressed as the percentage of patients without hemoptysis at least 30 days after the embolization<sup>1,14</sup>. The subsequent treatment (repeat BAE, emergency bronchoscopy, or surgery) for the cases of recurrent hemoptysis was determined using a multidisciplinary approach involving the emergency room doctor, the interventional radiologist, the pulmonologist, and the thoracic surgeon. The angiographic causes of recurrence were categorized (recanalization of embolized vessels, presence of other vessels causing missed hemoptysis, or bleeding from new collateral vessels) for the patients undergoing BAE following recurrent hemoptysis<sup>15</sup>. The embolization follow-up was defined in terms of time to hospital admission or date of death.

#### **Complications**

Each patient was followed up closely after the BAE intervention to identify any complications. Here, the CT scans, the bronchoscopy results, the CT findings related to pulmonary ischemia or pulmonary infarction, and the CT/bronchoscopic findings related to airway abnormalities (necrosis, bronchial stenosis, and broncho-esophageal fistula) documented in the electronic medical records of the emergency or outpatient clinic admission departments were used to evaluate the presence of late complications<sup>7,16,17</sup>. Here, compli-

cations requiring a prolonged hospital stay and advanced care or those resulting in permanent sequelae or death following BAE were defined as major complications<sup>7</sup>, with all other complications regarded as minor.

## Statistical Analysis

The data were analyzed using IBM SPSS version 23 (IBM Corp., Armonk, NY, USA) software, with the compliance of the qualitative data to a normal distribution examined using the Shapiro-Wilk test. Meanwhile, the normally distributed age-independent samples were analyzed *via t*-test, while the non-normally distributed hemoptysis volume and follow-up time values were examined using the Mann-Whitney U-test. Chisquare and Fisher's exact tests were used to compare the categorical data, which were presented in terms of frequency (percentage). The quantitative data were presented in terms of mean  $\pm$  SD and median (min-max), with p < 0.05 regarded as statistically significant.

#### Results

The gender distribution did not vary between the groups (p = 0.835), with the proportion of men in the glue-embolizing agent group (80%) and in the particulate embolizing agent group (82.1%). The etiological factor distribution indicated that 43.3% of the glue-embolizing agent group and 39.3% of the particulate-embolizing agent group were diagnosed with bronchiectasis. The CT examinations revealed that the distribution of the number of lung lobes with involvement did not differ between the groups (p = 0.315), while there was also no difference in the distribution of the embolized vessels (p = 0.350). The embolized vessel analysis revealed that the bronchial vessel rate was 70% for the glue-embolizing agent group, with a bronchial/non-bronchial vessel ratio of 30%, and 78.6% for the particulate embolizing agent group, with a bronchial/non-bronchial ratio of 17.9%.

Furthermore, the emergence of recurrent hemoptysis did not differ between the two groups (p = 0.097), with a recurrence rate of 3.3% in the glue group and 17.9% in the agent group. However, there was some difference in terms of the distribution of the causes of recurrent hemoptysis (p = 0.003).

Both technical and clinical success was achieved in all cases for both groups, with no

major complications. Meanwhile, certain minor complications were observed in only 10.7% of the cases in the agent group, with one patient experiencing inguinal hematoma and two experiencing transient chest pain.

A statistically significant difference was found in terms of the distribution of the localization of the disease (p = 0.038), with the localization found to be around the lower lobe of the right lung in 53.3% of the glue group and 17.9% of the agent group (Table I).

However, there were no statistically significant differences in the mean age values of the patients (p = 0.618), the median hemoptysis volume (p = 0.559), or the follow-up period (p = 0.523) (Table II).

#### Discussion

This retrospective study revealed technical and clinical success in all patients (100%) undergoing BAE using NBCA and particulate embolizing agents (microspheres/PVA). These results support those reported in previous studies<sup>5,7,9,15,18</sup> in relation to technical and clinical success rates.

Various agents, including absorbable gelatin sponge particles (gel-foam), PVA particles, microspheres, coils, and glue (NBCA), have been used for BAE procedures. Here, while gel foam is the most economical embolizing agent, advancing it through microcatheters with slight calibration is often difficult. Furthermore, the recurrent hemoptysis rate tends to be high due to proximal occlusion of the vessels and spontaneous recanalization of the arteries. Meanwhile, while coils are appropriate for actively bleeding vessels, such as in pseudoaneurysms, due to the permanent proximal occlusion of the vessels, they can complicate the later procedures carried out in view of possible recurrence<sup>19</sup>. In fact, microspheres and PVA remain the main particulate embolizing agents used in BAE procedures<sup>1,18,20</sup>. Here, spherical, uniform, regular, smooth-sided, and, therefore, non-absorbable microspheres have the advantage of preventing microcatheter occlusion during embolization. In contrast, PVA has a non-absorbable but non-uniform shape and, therefore, tends to agglomerate, which can cause catheter occlusion or proximal arterial occlusion during infusion.

Nonetheless, the high technical success rate using PVA particles has been reported in numerous studies<sup>1,7,21</sup>. Meanwhile, the main argument against using glue (NBCA) relates to the high risk

**Table I.** Group comparison in terms of categorical variables.

	Group 1 (NBCA) (n = 30)	Group 2 (particulate embolizing agent) (n = 28)	Total	Test statistics	P
Gender					
Male	24 (80)	23 (82.1)	47 (81)	$\chi^2 = 0.043$	0.835
Female	6 (20)	5 (17.9)	11 (19)	,,	
Etiology	. ,	, ,	. ,		
Unknown	4 (13.3)	4 (14.3)	8 (13.8)		
Bronchiectasis	13 (43.3)	11 (39.3)	24 (41.4)		
Tuberculosis	3 (10)	5 (17.9)	8 (13.8)		
Lung cancer	6 (20)	6 (21.4)	12 (20.7)		
Wegener's disease	0 (0)	1 (3.6)	1 (1.7)		
Church Straus syndrome	1 (3.3)	0 (0)	1 (1.7)		
Aspergillus	2 (6.7)	0 (0)	2 (3.4)		
Dieuloy's disease	0 (0)	1 (3.6)	1 (1.7)		
Bronchial fistula	1 (3.3)	0 (0)	1 (1.7)		
The extent of disease	(0.0)	· (*)	- ()		
(number of lobes involvements)					
1	14 (46.7)	17 (60.7)	31 (53.4)	$\gamma^2 = 3.541$	0.315
2	12 (40)	7 (25)	19 (32.8)	<i>/</i> C	
3	3 (10)	1 (3.6)	4 (6.9)		
4	1 (3.3)	3 (10.7)	4 (6.9)		
Embolized Vein	(0.0)	2 (2311)	(00)		
Bronchial	21 (70)	22 (78.6)	43 (74.1)	$\chi^2 = 2.100$	0.350
Bronchial and non-bronchial	9 (30)	5 (17.9)	14 (24.1)	,,	
Non-bronchial	0 (0)	1 (3.6)	1 (1.7)		
Recurrent hemoptysis	- (-)	()	( )		
No	29 (96.7)	23 (82.1)	52 (89.7)		$0.097^{\rm F}$
Yes	1 (3.3)	5 (17.9)	6 (10.3)		
Cause of recurrent hemoptysis	(0.0)	(2.13)	· ()		
Other culprit arteries are present	1 (3.3)	0 (0)	1 (1.7)	$\chi^2 = 14.301$	0.003
No	2 (6.7)	11 (39.3)	13 (22.4)	/ 01	
Recanalization	0 (0)	3 (10.7)	3 (5.2)		
No	27 (90)	14 (50)	41 (70.7)		
Technical success	(> 0)	(00)	(, 0,)		
Yes	30 (100)	28 (100)	58 (100)		
Clinical Success	20 (100)	20 (200)	50 (100)		
Yes	30 (100)	28 (100)	58 (100)		

 $<sup>\</sup>chi^2\!\!:$  Chi-square test,  $^F\!\!:$  Fisher's exact test.

**Table II.** Group comparison in terms of quantitative data.

	Glue	Particulate embolizing agent	Total	Test statistics	P
Age	$54.8 \pm 17.3$ 59.0 (18.0-84.0)	52.9 ± 11.8 55.5 (26.0-75.0)	53.9 ± 14.8 56.5 (18.0-84.0)	t = 0.501	.618
Hemoptysis volume	$488.3 \pm 217.6$	$490.0 \pm 178.4$	$489.1 \pm 197.9$	U = 383.0	.559
Follow-up duration (months)	425.0 (300.0-1,000.0) 30.7 ± 23.8 34.0 (1.0-85.0)	475.0 (300.0-1,000.0) 38.0 ± 31.9 33.5 (1.0-98.0)	450.0 (300.0-1,000.0) 34.2 ± 28.0 34.0 (1.0-98.0)	U = 379.0	.523

t: Two independent samples t-test statistics, U: Mann-Whitney U test statistic, mean  $\pm$  s. deviation, median (min-max).

of serious complications, such as tissue necrosis and the involuntary embolization of normal vessels secondary to uncontrolled reflux<sup>5</sup>. The widespread use of liquid embolic agents, especially

for treating cerebral and spinal arteriovenous malformations, has led to increased efficacy in controlling the behavior of such materials, and relevant data regarding their usage for BAE have also been reported<sup>5</sup>. In the present study, the embolization was carried out using particulate (microspheres/PVA) embolizing agents and NBCA, with no coil or gel foam used.

Contemporary scholarship has proposed that certain factors that must be carefully considered may increase the success rate when using NBCA. This includes what should be done to prevent reflux and the measures to prevent premature polymerization. Meanwhile, the various practitioners' NBCA-based techniques tend to differ<sup>5,22,23</sup>. Baltacıoğlu et al<sup>5</sup> applied an NBCA concentration of 12.5% to prevent early polymerization in BAE interventions, while Woo et al<sup>7</sup> applied NBCA concentrations of varying ratios from 1:2 to 1:4 for their patients undergoing embolization. Here, all the procedures were successful, with premature polymerization prevented, with the NBCA concentration rate varying from 12.5% to 25% depending on the distal advancement of the microcatheter and the vessel diameter or the width of the embolization area.

Traditionally, the most commonly used PVA rate has been 300-500 µm, while the post-2010 literature discusses a broader range of PVA particle rates of 150-1,200 µm<sup>18</sup>. Scholars<sup>18</sup> have also used microspheres with a size range of 100-900 μm and 250-1,300 μm in their embolization procedures. Corr<sup>24</sup> used 500-700-µm microspheres, while Kucukay et al1 performed embolization using a larger size of 700-900 µm. Larger particles have the advantage of preventing off-target embolization, as the primary goal in BAE procedures is to interrupt the abnormal-looking bronchial vascular arterial flow and stop the bleeding. The anterior spinal artery is the most crucial artery to be protected, meaning using particles smaller than 325 µm is not recommended<sup>1,25</sup>. No embolic agents with a diameter of less than 300 µm were used as the particulate embolic materials in this study, and no spinal cord injury or major procedure-related complications occurred.

The recurrent hemoptysis analysis indicated that the reported clinical and technical success rates in BAE interventions performed with different embolizing agents are varied. For example, Chun et al<sup>2</sup> achieved an 85% clinical success rate and observed a recurrent hemoptysis rate of 28% following embolization using PVA in 50 patients with moderate and massive hemoptysis, while Pei et al<sup>26</sup> achieved clinical success rates of up to 86.6%, with the clinical recurrence rate

24.1% for the embolization using gelatin Spongostan in 112 patients experiencing massive hemoptysis. Elsewhere, Fruchter et al<sup>27</sup> achieved a 92% clinical success rate and 57.5% clinical recurrence rate in their embolization procedure, embossing microspheres and coils in 52 patients with moderate and massive hemoptysis. In fact, high technical and clinical success rates have been achieved with the microsphere-based BAE procedures reported in the existing studies. Here, Corr<sup>24</sup> and Kucukay et al<sup>1</sup> achieved technical success rates of 90% and 100%, clinical success rates of 87% and 91.9%, and recurrent hemoptysis rates of 13% and 8.1%, respectively. Meanwhile, another study<sup>28</sup> demonstrated that no significant difference emerged in the recurrent hemoptysis rate in terms of PVA- and microsphere-based BAE with different embolic agents other than NBCA. Elsewhere, Baltacioglu et al<sup>5</sup> examined 25 patients following a glue (NBCA)-based procedure. Here, the hemoptysis was controlled immediately following the procedure in all 25 patients (100%) and in 24 patients (96%) at a one-month follow-up, with the authors reporting that the recurrent hemoptysis originated from another problem artery in one patient who was not embolized before the 10th day following embolization. Meanwhile, Woo et al<sup>7</sup> recently published a study on 406 patients, grouping the patients who underwent a BAE procedure in terms of PVA particles and NBCA. Here, the technical success rate was 93.9% (275/293) in the PVA group and 96.5% (109/113) in the NBCA group, while the one-, three-, and five-year hemoptysis-free survival rates were 77%, 68%, and 66% for the former and 88%, 85%, and 83% for the latter. Furthermore, the recanalization rate in the previously embolized vessels was reported to be 21.5% in the PVA group and 1.8% in the NBCA group. Thus, it was concluded that NBCA was better than PVA in preventing recurrent hemoptysis. Moreover, the vessel recanalization rate was significantly higher after PVA usage, while no statistically significant difference was observed between the groups regarding technical and clinical success rates.

However, in the present study, six patients with PVA usage, one with PVA/microsphere usage, 21 with microsphere usage, and 30 with NBCA usage were recruited. The technical and clinical success rate was 100% in both the particulate embolization group and the NBCA group. Recurrent hemoptysis was observed in one patient (3.3%) in

the NBCA group and five (17.9%) in the particulate embolizing agent (microspheres/PVA) group. The two groups had no statistically significant difference (p = 0.097). The cause of hemoptysis in the NBCA group was another newly developing problem vessel.

Meanwhile, recanalization was detected in all five patients with recurrent hemoptysis in the particulate embolizing agent group regarding the previously embolized problem vessel, and a new interventional procedure was performed. Previous studies<sup>5,6</sup> have demonstrated that NBCA is a safe and effective embolic agent with higher hemoptysis-free survival rates than when using particulate embolic agents such as PVA. No recanalization was observed in any patient embolized with NBCA usage and followed up for an average of 34 months in this study. However, there was no statistical difference in the recurrent hemoptysis rates. It can be concluded that NBCA is a more powerful agent in preventing recurrent hemoptysis, given that five patients embolized with a particulate embolizing agent had recurrent hemoptysis due to recanalization within the first year. In fact, NBCA can be used in BAE, especially in the early stages, due to the controlled nature of the recanalization technique. Specific differences, specifically in relation to the higher technical and clinical success rates, differentiate this study from previous attempts. We believe these differences can be attributed to the embolizing agents, etiological factors, and super-selective or selective catheterization. It can be proposed that super-selective catheterization in both NBCA and particulate embolizing agent usage and the high level of experience of the practitioners are essential factors in increasing the technical and clinical success rates.

The most common complications in the BAE interventions were transient chest/back pain and dysphagi7,18,29,30, while post-embolization syndrome with fever, leukocytosis, and pain were other common and self-limiting complications<sup>7,18,29,30</sup>. Meanwhile, contrast allergies, inguinal hematomas, and femoral artery pseudoaneurysms at the puncture site were also reported<sup>7,18,30</sup>, while wire or catheter-related vascular injuries, such as vasospasm and perforation, were reported in 0.3%-13% cases, leading to the technical failure of the BAE<sup>18,29,30</sup>. Transient ischemia/stroke and cortical blindness due to subclavian artery manipulation or bronchopulmonary anastomoses were reported with a minimal range of 0.6-2% while temporary or permanent paraparesis or paraplegia was detected in 0.6%-4.4% of cases, which was largely due to spinal cord ischemia caused by involuntary embolization of the spinal artery originating from the bronchial or intercostobrachial arteries<sup>4,18,29</sup>. Minor complications were identified in only three patients, with inguinal hematoma emerging in one patient and transient chest pain in two. However, there were no major complications in either group.

#### **Limitations**

This study also has certain limitations, with the retrospective design of the study representing a primary concern. The fact that the study was conducted with a limited number of patients did not allow for performing subgroup analyses. Furthermore, the factors behind certain long-term outcomes, such as antibiotic use, blood oxygen levels, and malignancy-related radiation effects, were omitted. Finally, the choice of NBCA or particulate embolizing agent was determined according to the preference and experience of the interventional radiologist, which increased the risk of serendipity and may have led to some bias in the results.

#### Conclusions

Overall, this study demonstrated that using NBCA in BAE procedures presents a safe and effective method. The combination of NBCA and particulate embolizing agents (PVA/microspheres) achieved equal technical and clinical success rates and significantly increased the hemoptysis-free survival rates in relation to life-threatening hemoptysis. Neither major complications nor procedural death occurred in either of the samples. Furthermore, there was no evidence of increased complications associated with NBCA, while tissue ischemia and off-target embolization were expected. However, the results must be validated through conducting larger multicenter and well-randomized studies.

### **Conflict of Interest**

The authors declare that they have no conflict of interests.

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#### Authors' Contribution

M. Mazıcan, I. Karluka, C. Andıc; concept, design, supervision, data collection, literature search, writing manuscript, critical review, analysis and interpretation, and resources and editing. A. Fındıkcıoglu; concept, design, data collection, analysis, literature review, manuscript writing, critical review, resources and materials.

#### **Ethics Approval**

This study was conducted in accordance with the principles of the Declaration of Helsinki. This study was approved by the Baskent University Institutional Review Board (Project No.: KA20/349).

#### **Informed Consent**

A written informed consent was obtained from patients at enrolment to include them in registries and make their data available for subsequent analysis. Yet, oral informed consent for inclusion in this study was further obtained from patients or relatives (in the case of dead patients) during follow-up telephone calls.

#### **Data Availability**

All data used in this study can be obtained from the author upon request.

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