

Angiographic Findings and Outcomes of Bronchial Artery Embolization in Patients with Pulmonary Tuberculosis

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ABSTRACT

Objective: We aimed to evaluate the angiographic findings and outcomes of bronchial artery embolization in tuberculosis patients and to compare them with those of non-tuberculosis patients.

Materials and Methods: Patients who underwent bronchial artery embolization in a single interventional radiology department with hemoptysis were reviewed. A total of 89 patients (66 males and 23 females; mean age 52.71 ± 15.37) were incorporated in the study. The patients were divided into two groups: tuberculosis group (n=36) and non-tuberculosis group (16 malignancy, 22 bronchiectasis, 6 pulmonary infection, 5 chronic obstructive pulmonary disease, 4 idiopathic; n=53). Angiography and embolization procedure were performed by interventional radiologists with 5, 10, and 20 years of experience. Angiographic findings were classified as tortuosity, hypertrophy, hypervascularity, aneurysm, bronchopulmonary shunt, extravasation, and normal bronchial artery. Chi-square test was used to compare angiographic findings between tuberculosis and non-tuberculosis patient groups.

Results: Bronchopulmonary shunt was found to be significantly higher in the tuberculosis group as compared to that in the non-tuberculosis group ($p=0.002$). Neither of the groups showed a statistically significant difference with respect to recurrence ($p=0.436$).

Conclusion: Bronchial artery embolization is a useful and effective treatment method of hemoptysis in tuberculosis. Evaluation of bronchopulmonary shunts in patients with tuberculosis is critical for the reduction of catastrophic complications.

Keywords: Embolization, digital subtraction angiography, hemoptysis, treatment outcome, tuberculosis.

Introduction

Hemoptysis is a common and sometimes life-threatening symptom that may have many underlying etiologies. It is defined as the expectoration of blood from the respiratory system [1]. If hemoptysis is massive (>300 mL per day) and untreated, the mortality rates may rise to 50% [2]. Management of hemoptysis includes conservative treatment, surgery, and bronchial artery embolization (BAE). Patients admitted with massive hemoptysis are usually in poor condition medically and cannot tolerate surgery. In addition, serious complications such as asphyxia, bronchopleural fistula, and respiratory failure may occur in patients who undergo surgery [1]. Therefore, BAE has become the primary treatment method of massive or intermittent-moderate (>100 mL per day) hemoptysis [3, 4].

The causes of hemoptysis vary significantly between developed and non-developed countries. In non-developed countries, tuberculosis is the most frequent cause of massive hemoptysis [5]. Since Remy et al. [6] first described BAE for the management of hemoptysis, several studies have declared the efficacy of BAE in tuberculosis patients [7-11]. These studies have investigated the outcomes of BAE in tuberculosis patients and the risk factors that affect recurrence. However, angiographic findings and their influence on the embolization procedure are not reported in detail.

The aims of this study were to evaluate angiographic findings during BAE in tuberculosis patients and to compare the findings with those of non-tuberculosis patients. We also tried to reveal the effect of angiographic pattern on the success and technique of BAE.

Materials and Methods

Local ethics committee approval was obtained for this retrospective study. One hundred and five patients who underwent BAE between August 2015 and July 2018 in a single interventional radiology department with moderate (>100 mL per day) or severe (>300 mL per day) hemoptysis refractory for medical and bronchoscopic treatment were reviewed. In 16 patients, no pathologic artery was found during the angiography, so they were excluded from the study. A total of 89 patients (66 males and 23 females; mean age 52.71 ± 15.37) were incorporated in the study. The patients were divided into two groups according to their diagnosis: tuberculosis group (n=36) and non-tuberculosis group (16 malignancy, 22 bronchiectasis, 6 pulmonary infection, 5 chronic obstructive pulmonary disease, 4 idiopathic; n=53). The diagnosis of tuberculosis was made by experienced pulmonologists after reviewing medical history, laboratory findings, acid-fast bacilli (AFB) smear, and a radiologic examination. Tuberculosis patients were subdivided into active and latent groups. Active disease was classified as primary and post primary (reactivation) tuberculosis [12]. Patients, who had not been previously exposed to *Mycobacterium tuberculosis*, with clinical (cough, hemoptysis, fatigue, malaise, weight loss, fever, night sweats), radiological (lymphadenopathy, consolidation, pleural effusion, miliary nodules), and laboratory (AFB-positivity) findings were considered as primary tuberculosis patients [13]. Patients who met the criteria for an active clinical case and AFB-positivity, with accompanying radiologic findings (consolidations predominant in the apical and upper lung zones, nodules, cavitations) were considered as reactivation tuberculosis patients [14]. Patients with AFB-negativity but having radiologic or clinical evidence of former tuberculosis were classified as latent tuberculosis patients [12]. Multi-drug resistant tuberculosis was defined as the resistance to isoniazid and rifampin therapy in culture studies [13].

Written informed consent was obtained from all patients prior to embolization. Angiography and embolization procedures were performed

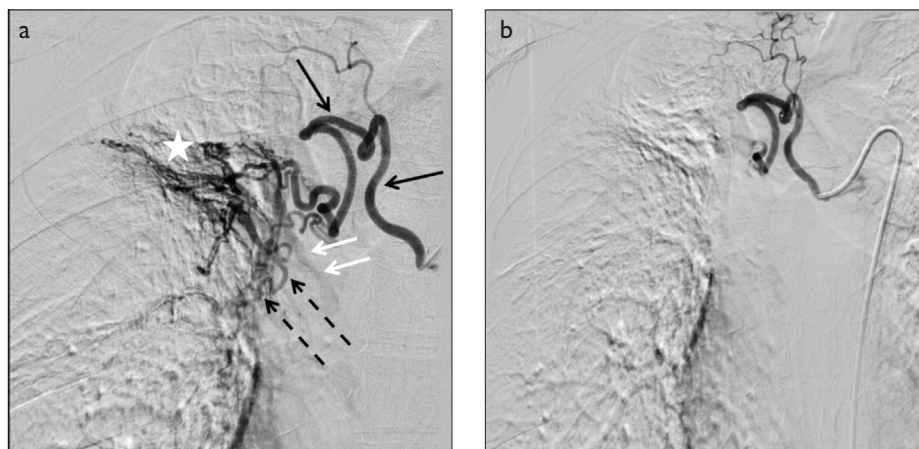


Figure 1. a, b. a) Hypertrophy (black arrows), hypervascularity (star), tortuosity (dotted arrows), bronchopulmonary shunt (white arrows) are seen in the pathologic bronchial artery on a selective right intercostobronchial trunk angiogram. b) Postembolization angiogram demonstrates the cessation of antegrade flow.

by interventional radiologists with 5, 10, and 20 years of experience with a classical method that has been previously described [15]. Before the procedure, a computed tomography (CT) of the thorax and a bronchoscopy were performed on all patients to find the pathologic lesion and artery. Common femoral artery was chosen for access under ultrasound guidance. The decision for embolization and selection of embolic agents were made by the operators during the procedure. After inserting a 5-French sheath into the common femoral artery, a thoracic aortogram was taken with a 5-French pigtail catheter to distinguish any abnormal sites and assess the origin of the bronchial and non-bronchial systemic arteries. In all patients, internal thoracic, subclavian, and intercostal arteriograms in addition to bronchial arteriograms were performed to observe any abnormal contrast filling. Simmons I and Cobra 2 catheters were used to find the origin of the pathologic arteries. Hand injection was used in selective bronchial or non-bronchial angiograms. After observing an abnormal angiographic finding, a microcatheter (Renegade microcatheter; Boston Scientific, Natick, Massachusetts) was advanced superselectively to the pathologic artery. Embolization was done after obtaining a superselective angiogram and after evaluating the angiographic findings. Microparticles $\geq 500 \mu\text{m}$ were used if there was a bronchopulmonary shunt. In other cases, embolization started with $350 \mu\text{m}$ sized microparticles to achieve complete embolization of the distal vascular territory. Microspheres (Embozene; Boston Scientific, Cork, Ireland) sized between $350\text{--}700 \mu\text{m}$ diameter were used as embolic agents. Embolization was ended when there were a significant contrast material stasis and no antegrade flow. Coils were not used to avoid

any access difficulties in the case of possible recurrence.

We classified angiographic findings as tortuosity, hypertrophy, hypervascularity, aneurysm, bronchopulmonary shunt, extravasation, and normal bronchial artery (Figure 1) [16]. Tortuosity referred to more than two turns in opposite directions of the pathologic artery. Hypertrophy meant that the diameter of the anomalous artery is greater than 3 mm. Hypervascularity meant increased contrast filling with parenchymal blush and staining. Aneurysm referred to a localized dilation of the diseased artery. Bronchopulmonary shunt was described as contrast material flowing from systemic circulation into the pulmonary circulation. When no pathologic finding was seen, the artery was considered as “normal”.

Angiographic findings of the diseased arteries were evaluated by two interventional radiologists with 5 and 10 years of experience. All patient data were hidden during the analysis. In cases of disagreement between the two interventional radiologists, the images were reevaluated. Furthermore, a third interventional radiologist (U.B.) with 20 years experience reanalyzed the images, and the final decision was reached by consensus.

Technical success, clinical success, recurrence rates, and minor and major complication rates were considered during the outcome analysis. Technical success was described as rapid interruption of blood flow from the diseased artery [17]. Clinical success was defined as the total cessation of hemoptysis. Partial recovery that did not need any medication within a minimum of 30 days was also referred as clinical suc-

Main Points

- Bronchial artery embolization is a safe and effective treatment method for hemoptysis in patients with tuberculosis.
- Bronchopulmonary shunt was significantly higher in tuberculosis patients compared to the non-tuberculosis group.
- There was no difference in the angiographic findings between reactivation and latent tuberculosis.



Figure 2. Right intercostobronchial arteriogram demonstrates hypervascular areas and extravasation (black arrow) in the right upper lobe



Figure 3. Patient referred with hemoptysis after right intercostobronchial trunk embolization. Right costocervical trunk angiogram shows the hypervascular lesion with hypertrophy and tortuosity

Table 1. Angiographic findings of tuberculosis and non-tuberculosis patients

Findings	Total number of patients (n=89)	Tuberculosis group (n=36)	Non-tuberculosis group (n=53)	p value
Hypervascularity				
Absent	4 (4.5%)	1 (2.8%)	4 (7.5%)	0.537
Present	85 (95.5%)	35 (97.2%)	50 (92.5%)	
Hypertrophy				
Absent	19 (21.4%)	6 (17.1%)	13 (24.5%)	0.410
Present	70 (78.6%)	30 (83.3%)	40 (75.5%)	
Tortuosity				
Absent	9 (10.2%)	1 (2.8%)	8 (15.1%)	0.064
Present	80 (89.8%)	35 (97.2%)	45 (84.9%)	
Shunt				
Absent	58 (65.2%)	17 (47.2%)	41 (77.4%)	0.002
Present	31 (34.8%)	19 (52.8%)	12 (22.6%)	
Aneurysm				
Absent	84 (94.4%)	33 (91.7%)	51 (96.2%)	0.341
Present	5 (5.6%)	3 (8.3%)	2 (3.8%)	
Normal bronchial artery				
Absent	80 (89.9%)	35 (97.1%)	45 (84.9%)	0.064
Present	9 (10.1%)	1 (2.9%)	8 (15.1%)	
Extravasation				
Absent	88 (98.9%)	35 (97.3%)	0 (0%)	N/A
Present	1 (1.1%)	1 (2.7%)	0 (0%)	

as percentages. The distribution of continuous variables was evaluated by the Kolmogorov-Smirnov or the Shapiro-Wilk test. The independent t-test or Mann-Whitney U test was used for the comparison of age and the angiographic findings. The chi-square test or Fisher's Exact test was used to compare angiographic findings between the tuberculosis and non-tuberculosis groups, between reactivation and latent groups of patients with tuberculosis, and to assess the relationship between recurrence rates and angiographic findings. P-values of less than 0.05 were considered statistically significant.

Results

Among 89 patients, 36 had tuberculosis (16 latent, 20 active) and 53 did not have tuberculosis. The tuberculosis group consisted of 34 men (94.4%) and 2 women (5.6%) with a mean age of 49.57 ± 17.75 . There were 32 males (60.4%) and 21 (39.6%) females in the non-tuberculosis group (mean age 54.57 ± 13.45). There was a significant difference in the gender of patients between the two groups ($p < 0.001$). All active tuberculosis patients consisted of reactivation tuberculosis patients. Among the reactivation group, two of the subjects were found to have multi-drug resistant tuberculosis.

A total of 98 embolization procedures were performed in 89 patients. The angiographic findings of all patients are presented in Table 1. Tortuosity and hypervascularity were the most common findings in the tuberculosis (both reactivation and latent) and non-tuberculosis groups. Among all patients, extravasation was the rarest observation, and it was observed in only one case with a reactivation tuberculosis patient (Figure 2). Aneurysm was the second least common observation in both the tuberculosis and non-tuberculosis groups. No significant correlation was observed between age or gender and any of the angiographic findings. Angiographic findings in tuberculosis and non-tuberculosis groups are summarized and compared in Table 1. No significant relationship was found between age or gender and angiographic findings in tuberculosis patients. Bronchopulmonary shunt was found to be significantly higher in tuberculosis patients compared to the non-tuberculosis group ($p = 0.002$); 19 of 36 (52.8%) patients with tuberculosis had bronchopulmonary shunt; however, in the non-tuberculosis group, only 12 of 53 (22.6%) had a shunt. Angiographic findings of tuberculosis patients and comparisons are summarized in Table 2. No significant differences in angiographic findings were found between the tuberculosis reactivation and tuberculosis latent groups ($p > 0.05$). The number of embolized arteries

cess [18]. The requirement of medical, surgical, or angiographic treatment for hemoptysis after embolization was regarded as recurrence. Follow-up information was obtained from inpatient and outpatient records retrospectively. Extended hospitalization, irreversible sequelae, or death were regarded as major complications. Minor complications such as hematoma at the access site were conditions that did not result

in sequelae and needed only minimal care and observation [19].

Statistical Analysis

Statistical analysis was performed by using the Statistical Package for the Social Sciences version 22.0 (IBM Corp.; Armonk, NY, USA). Continuous data were expressed as means \pm standard deviation (SD) and categorical variables

Table 2. Angiographic findings of tuberculosis patients

Findings	Reactivation tuberculosis (n=20)	Latent tuberculosis (n=16)	p value
Hypervascularity			
Absent	1 (5%)	0 (0%)	1
Present	19 (95%)	16 (100%)	
Hypertrophy			0.666
Absent	4 (20%)	2 (12.5%)	
Present	16 (80%)	14 (87.5%)	
Tortuosity			1
Absent	1 (5%)	0 (0%)	
Present	19 (95%)	16 (100%)	
Shunt			0.740
Absent	8 (40%)	8 (50%)	
Present	12 (60%)	8 (50%)	
Aneurysm			0.582
Absent	19 (95%)	14 (87.5%)	
Present	1 (5%)	2 (12.5%)	

Table 3. Number of embolized arteries and origins of the pathologic artery in tuberculosis and non-tuberculosis group

Origin of the embolized arteries	Tuberculosis group (n=57)		Non-tuberculosis group (n=71)	
	n	%	n	%
Bronchial	39	68.5	54	76.1
Intercostal	11	19.3	12	16.9
Subclavian	4	7.0	2	2.8
Inferior phrenic	0	0	2	2.8
Internal thoracic	3	5.2	1	1.4

Table 4. Degree of hemoptysis and recurrence rates

	Tuberculosis group (n=36)	Non-tuberculosis group (n=53)
Degree of hemoptysis		
Moderate	17 (47.2%)	31 (58.5%)
Massive	19 (52.8%)	22 (41.5%)
Recurrences		
<30 days	3 (8.3%)	1 (1.9%)
>30 days	3 (8.3%)	5 (9.4%)

and origins of the embolized artery are shown in Table 3. In the tuberculosis group, 68.5% of the arterial abnormality was observed in the bronchial system. In the non-tuberculosis group, 76.1% of the pathologic arteries originated from the bronchial arteries.

The mean follow-up period in this study was 17.09 months \pm 9.16 (range 1-36 months; median 18 months). A total of 128 arteries were embolized in 98 procedures; one artery

in 55 patients (19 in tuberculosis, 36 in non-tuberculosis), two arteries in 29 patients (16 in tuberculosis, 13 in non-tuberculosis), three arteries in 5 patients (2 in tuberculosis, 3 in non-tuberculosis). Pathologic arteries could not be embolized in two procedures due to the challenging angles from the aorta. Thus, our overall technical success rate was 98% (98/100). Clinical success rate was recorded as 91.6% (33/36) among tuberculosis group and 98.1% (52/53) among non-tuberculosis

group. The overall clinical success rate was 95.5% (85/89). No major complication was experienced. Short-lasting chest pain occurred in one patient (1/89, 1.1%) and stopped during monitoring. Bronchial artery spasm occurred in three patients (3/89, 3.3%) and bronchial artery dissection appeared in four patients (4/89, 4.4%).

Recurrence rates and the degree of hemoptysis are outlined in Table 4. Recurrence occurred in 12 of the 89 patients (13.4%). In the tuberculosis group, 6 patients (3 latent, 3 reactivation) required reembolization; and 6 patients in the non-tuberculosis group also underwent reembolization due to recurrent hemoptysis. No relationship was found between the severity of hemoptysis and recurrence ($p>0.05$). None of the groups showed a statistically significant difference with respect to recurrence ($p=0.436$). Also, neither reactivation nor latent groups were associated with significantly higher recurrence rates. Among the tuberculosis group, reembolization was performed after 8 months for one patient, after 4 months for another, after 3 months for the third, and within the first month for three patients. Clinical failure was seen in three patients with tuberculosis within one month. Of these three patients, two underwent reembolization due to recanalization of the same vessels. No abnormality was found during angiography in the last patient, thus medical treatment was given. Among the three patients who developed recurrence after one month had passed, recanalization with collaterals was observed in one (Figure 3). Pathologic arteries different from the ones observed in the first procedure were seen and embolized in the remaining two patients. There was no significant relationship between angiographic findings and recurrence in tuberculosis patients ($p>0.05$). Among non-tuberculosis recurrence group ($n=6$), reembolization was performed after 16 days (chronic obstructive pulmonary disease), 8 months (malignancy), 13 months (bronchiectasis), 18 months (bronchiectasis), 22 months (malignancy), and 31 months (bronchiectasis). In the clinical failure case within the first month, recanalization of the same vessel was observed during the procedure. Different arteries were the cause of hemoptysis in the remaining five cases.

Discussion

Our study demonstrated that hypervascularity and tortuosity were the most common angiographic findings in tuberculosis patients. Bronchopulmonary shunt was significantly higher in the tuberculosis group compared to that in the non-tuberculosis group.

Continuous airway inflammation, bacterial superinfection, cavities, scar lesions, bronchiectasis, and erosion of the adjacent vessels may be possible reasons of vascular rupture in tuberculosis [13]. Chronic inflammation induces localized hypoxia and subsequent reduction in the pulmonary flow. Various angiogenic growth factors occur to supply adequate perfusion to the lungs. Neovascularization aggravates the fragility of vessels and eventually hemorrhaging occurs [20].

As a consensus, tortuosity, hypervascularity, hypertrophy, bronchopulmonary shunt, bronchial artery aneurysm, and active contrast extravasation are the main pathologic signs that need to be carefully examined during embolization in patients with pulmonary tuberculosis. In patients with tuberculosis, tortuosity and hypervascularity were the most prevalent results similar to those obtained by Dabo et al. and Anuradha et al. [10, 21]. Contrast extravasation, which is a direct sign of bleeding, is a rare angiographic finding in BAE [5]. In parallel with this condition, we only observed contrast extravasation in one patient during the procedure. Bronchopulmonary shunt seemed to be a common angiographic finding in tuberculosis similar to what was observed by Shin et al. [9]. There was no statistically significant difference in the angiographic findings between the tuberculosis and non-tuberculosis groups, except for bronchopulmonary shunting.

Bronchopulmonary shunts are connections between bronchial and pulmonary arteries or bronchial arteries and pulmonary veins. Vascular proliferation, remodeling, and collaterals can be seen between bronchial and non-bronchial systemic arteries occasionally. However, bronchopulmonary shunts may occur only in some conditions such as chronic inflammatory processes, malignancies, or decreases in the pulmonary flow (chronic thromboembolic pulmonary hypertension and congenital pulmonary stenosis) [22, 23]. As a consequence of shunting, pressure and circulation in the affected area augments and leads to hemoptysis [24].

The detection of bronchopulmonary shunts is vital to prevent the passage of the embolic agent into the pulmonary system in the presence of a bronchopulmonary shunt [25]. To avoid either pulmonary or systemic infarction, >325 µm sized particles are suggested for use [5]. During BAE in patients with tuberculosis, the presence of a bronchopulmonary shunt should be scrutinized to avoid severe complications. Furthermore, if a bronchopulmonary shunt is seen in an urgent BAE procedure with massive hemoptysis and unknown diagnosis, tuberculosis

may be considered as the underlying cause. The operator may suggest the clinician search for tuberculosis in such conditions. Anuradha et al. [10] reported that bronchopulmonary shunts were common in patients admitted with re-bleeding. No statistical significance was observed between bronchopulmonary shunt and recurrence in our study. However, manifested bronchopulmonary shunts were detected in two clinical failure cases in the tuberculosis group.

In the tuberculosis group, 32% of the bleeding source was the non-bronchial system. Intercoastal (19.3%) and subclavian (7%) arteries were the leading origins in the non-bronchial system. Ramakantan et al. [7] reported similar rates in intercoastal arteries. We found higher rates of pathologic subclavian and internal thoracic arteries with rates of 7.0% and 5.2%, respectively. According to our results, searching for potential non-bronchial systemic vessels is critical for appropriate treatment as there is a high rate of non-bronchial origin. Additionally, it was reported that embolization of non-bronchial systemic collaterals decreased the recurrence rates [10].

We showed that BAE was a secure, efficient, and functional method for controlling hemoptysis in both tuberculosis or other underlying diseases with a clinical success rate of 91.6% and 98.1%, respectively. These rates were similar to those of Lee et al. and Swanson et al. [26, 27]. The clinical success rates ranged from 70-99% in the literature [28]. Technical success rates of BAE had a wide range between 81-100% [21, 29, 30]. Clinical success rates were higher in the non-tuberculosis group than the tuberculosis group in the present study. This may be due to inadequate embolization of collaterals, rapid recanalization of the embolized artery, or conservatively unstoppable progression of the disease. Although angiographic findings were not associated with clinical success or recurrence, they manipulated the technique of embolization. Greater than 350 µm sized particles were used when bronchopulmonary shunts were observed.

The main reasons of recurrence are speculated to be incomplete embolization, recanalization of the embolized arteries, development of new collaterals, or progression of the underlying disease [9, 26, 29]. The studies investigating recurrence associated factors in tuberculosis after BAE had conflicting results. Hwang et al. [31] showed a statistical difference in bronchopulmonary shunt between the recurrence and non-recurrence groups. Contrary to this, Shin

et al. [9] assessed the relationship between angiographic findings and recurrence in tuberculosis patients but found no statistical significance. Furthermore, Anuradha et al. [10] did not notice any significant difference between recurrence and any angiographic or clinical feature in tuberculosis. Similarly, no significant relationship was found between angiographic findings and recurrence in the present study. Some studies showed that the recurrence rate was significantly higher in reactivation tuberculosis [9, 26]. However, we did not observe any difference between the reactivation and latent groups.

Major complications usually occur because of unintentional embolization of spinal arteries, manipulation of subclavian arteries, or transition of embolic agents through bronchopulmonary shunts. Agmy et al. reported monoparesis in 2 out of 348 patients [32]. Fruchter et al. [33] declared transient neurological complication rates as 4.4%. No neurologic symptoms occurred after embolization in our cases. The incidence of minor complications such as transient chest pain, arterial vasospasm, and dissection were compatible with the findings in the literature. Although groin hematoma and femoral artery pseudoaneurysms were also reported after BAE procedures [34, 35], we did not observe these problems. It may be due to the ultrasound-guided puncture of the common femoral artery.

The study had some limitations. The retrospective study design was a major limitation of the present study. Additionally, because of the relatively small sample size of the tuberculosis group, the number of patients with tuberculosis who had re-bleeding after embolization was too small. Further prospective studies with a larger number of patients are advisable.

In conclusion, BAE is a useful and effective treatment method for moderate and massive hemoptysis in tuberculosis. The occurrence of bronchopulmonary shunts seemed to be significantly higher in patients with tuberculosis. A detailed investigation of bronchopulmonary shunts in patients with tuberculosis during BAE is critical for both effective treatment and reduction of catastrophic complications.

Ethics Committee Approval: Ethics committee approval was received for this study from Tepecik Education and Research Hospital (14/11/2018, 2018/13-6).

Informed Consent: Written Informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - O.S., A.E.C.; Design- O.S., U.B.; Supervision- U.B.; Resources - O.S., A.E.C., M.Y.Y.; Materials - O.S., U.B.; Data Collection and/or Processing - A.E.C., M.Y.Y.; Analysis and/or Interpretation - O.S., M.Y.Y.; Literature Search - O.S., A.E.C., M.Y.Y.; Writing Manuscript - O.S.; Critical Review - U.B.

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