Pulmonary Arteriovenous Malformation in the Korean Population: Clinical Manifestations and the Long-Term Results of Transarterial Embolotherapy

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Purpose: This study was designed to evaluate the general features and the long-term results of transarterial embolotherapy (TAE) for the treatment of pulmonary arteriovenous malformations (PAVMs).

Materials and Methods: Thirteen [n=13] patients who underwent TAE for PAVMs were identified. These patients were comprised of 4 men and 9 women, aged between 19 and 67 years [mean age, 44 years]. The authors evaluated the general features of PAVMs, including, type, location, size, and symptoms. In addition, results following TAE were analyzed to evaluate its efficacy, and to investigate arterial oxygen pressure changes.

Results: In total, 13 patients presented with 21 angiographically confirmed PAVMs. Nine (69.2%) patients had single PAVM. Of the 21 PAVMs, 19 were simple, 16 were located in lower lobes, and 17 were located in the subpleural region. Furthermore, 2 of the 13 patients experienced coughing, 2 experienced dyspnea, and 1 experienced massive hemoptysis. All PAVMs were subjected to superselective TAE using a detachable balloon or coils. Six PAVMs (28.6%) in three patients (23.1%) were subsequently recanalized as determined by contrast-enhanced CT scan. All 3 patients were identified during long-term follow up (mean: 61.9 months). One of the 3 patients experienced an acute stroke due to thrombi migration in the middle cerebral artery following PAVM recanalization.

Conclusion: TAE with coils is effective for the treatment of PAVMs, and it should be noted that patients who undergo embolotherapy require careful surveillance, due to the need for recanalization during follow-up.

Index words: Arteriovenous Malformation
Embolization
Therapeutic
Pulmonary Artery
Pulmonary arteriovenous malformations (PAVMs) are abnormal direct communications between pulmonary arteries and veins without an intervening capillary network [1, 2]. PAVMs have been described in studies on the Caucasian population as being associated with hereditary hemorrhagic telangiectasia in 60–90% of cases [1–4], and have been reported in as many as 15–35% of patients with hereditary hemorrhagic telangiectasia (HHT) [2–5]. However, only case studies have been reported in Korea [6, 7], and no report has described the general features and long-term results of transarterial embolotherapy (TAE). Accordingly, this study was designed to evaluate the general features of PAVMs, and the long-term results of TAE.

**Materials and Methods**

**Patients**

The clinical records of all patients with confirmed PAVM who had undergone embolization from January 1992 to January 2008 were evaluated retrospectively. An institutional review board exemption was obtained for this study. During this period, 13 patients who underwent embolization were identified. The patients were comprised of 4 men and 9 women of aged between 19 and 67 years (mean age, 44 years). In 5 patients, PAVMs were diagnosed because of chest symptoms, such as, cough, dyspnea, or hemoptysis, and the other 8 were diagnosed during health screening chest radiography.

The imaging evaluations conducted before TAE were chest radiographs and/or computed tomography (CT). During the time of this study, a diagnosis of HHT was made if a patient had any two of the followings: recurrent spontaneous epistaxis, multiple telangiectases, visceral involvement with vascular malformation, and an autosomal-dominant inheritance pattern [8]. A consensus article from 2000 years [9] stipulates a definitive diagnosis be made if 3 of these clinical criteria are present, and that a possible or suspected diagnosis be made if 2 are present. Each patient was monitored clinically before and after embolization, specifically for signs and symptoms. In addition, routine laboratory examinations, such as live function tests, blood chemistry, complete blood count, prothrombin time, and activated partial thromboplastin time were performed.

**Embolization Technique**

Diagnostic pulmonary angiography was performed using the transfemoral vein approach in accordance with standard catheterization techniques, to place a pigtail catheter sequentially in the main pulmonary artery to each lung. Particular attention was paid to the branching pattern of the artery leading to the PAVM. A PAVM with one artery entering the aneurysm and a single draining vein was termed a simple PAVM, and a PAVM with two or more arteries or draining veins was classified as a complex PAVM [1].

In 12 patients a coaxial catheter system was used for coil embolization, and in the remaining 1 a detachable balloon was used. A 5 French introducer catheter (Headhunter, 125 cm in length; Cook, Bloomington, USA) was used to provide support across the heart and the pulmonary artery, and an inner 3-French microcatheter (Microferret; Cook, Bjaeverskov, Denmark) was used to perform finer selective maneuvers. Selective angiograms were then obtained using the 5-French catheter. The feeding artery was identified and catheterized superselectively in patients using a coaxially placed 3-French microcatheter (Microferret; Cook, Bjaeverskov, Denmark), which was advanced through a 5-French catheter using a 0.016-inch guide wire (GT; Terumo, Tokyo, Japan). Embolization through a 3-French microcatheter was achieved with microcoils or micronester. In the patient embolized with a detachable balloon, the procedure was conducted through a 5-French catheter. The distal aspects of the feeding arteries for embolization were occluded with a detachable balloon.

The embolic materials used included a detachable gold valve latex balloon \( n = 1 \); Boston Scientific, Natick, USA), microcoils \( n = 12 \); Tornado, Cook, Bjaeverskov, Denmark) or micronester coils \( n = 1 \); Cook, Bloomington, USA). We used coils of nominal diameters that were 10–20% larger than the estimated diameters of the feeder arteries. After embolizing the feeding arteries, segmental or lobar angiography was performed to assess adequate occlusion, and to identify any accessory feeding vessels that might also require embolization.

**Data Analysis and Follow-up**

We evaluated the general features of PAVMs using initial CT scans in terms of size and location in the lung, that is, subpleural, middle, or central portion. The mean follow-up time was 64.2 months \( \text{range, 7–168 months} \). CT scans \( \text{mean, 61.9 months} \) were obtained from follow-up studies \( \text{B-7} \). CT scans of the chest were obtained using either a single-section technique (Somatom
plus 4; Siemens, Munich, Germany) or using a 16-channel multidetector CT (MDCT) (Sensation 16; Siemens, Munich, Germany). Pre- and post-treatment CT scans were compared to assess persistence, and changes or resolutions of aneurysms and draining venous components. Successful treatment was defined as complete resolution of aneurysms and venous components, or reduction in aneurysmal or venous size of at least 70% by CT, as previously described by Lee et al. (10).

Recanalization was defined as no change, or enlargement in PAVM size, as depicted by follow-up CT, or when a PAVM showed contrast enhancement by follow-up enhanced CT. PAVMs that showed contrast enhancement were further evaluated using pulmonary angiography.

The paired Student t-test was used to analyze differences in pre- and post-treatment SPO2 values. Comparisons between two groups— one group that received reperfusion and a second group that did not were analyzed with the Student t-test or chi-square analysis.

**Fig. 1.** A 19-year-old woman with 4 incidentally found PAVMs. A-D. A superselective angiogram through a 3-F microcatheter shows four PAVMs (arrows) in both lungs (A; 19-mm size, complex type, B; 15-mm size, simple type, C; 5-mm size, simple type, D; 3-mm size, simple type). E, F. No residual filling of these four PAVMs are observed by final angiography after coil placement.
where appropriate. \( P < 0.05 \) was considered to indicate a statistically significant difference.

**Results**

**Initial Findings and Embolic Effects**

Patient and PAVM characteristics before and after TAE are shown in Table 1. Thirteen (\( n = 13 \)) patients with 21 angiographically confirmed PAVMs were identified. Of these 13 patients, 9 (69.2\%) had single PAVM and 4 had multiple PAVMs. Of the 21 PAVMs identified, 19 (90.5\%) were simple and two were complex. In terms of location, 16 PAVMs were located in the lower lobes (76\%), 17 in the subpleural region (81\%), 3 in the central region and 1 in the middle region. Of the 13 patients, 8 were asymptomatic, 2 experienced coughing, 2 experienced dyspnea, and 1 experienced massive hemoptysis. Only 1 patient with massive hemoptysis had a symptom attributable to PAVM. Routine laboratory test findings for all patients were normal.

All PAVMs were successfully embolized at first attempt. The mean arterial blood partial pressure of oxygen in the supine position before and after embolotherapy did not change significantly (\( p = 0.40 \)), and no immediate procedure-related complications were encountered.

**Follow-Up Findings**

The general features of 3 patients (with six reperfused PAVMs) before TAE are presented in Table 2. The data collected beyond the follow-up period are presented descriptively without statistical analysis. The feeding artery diameter and the proportion of multiple or complex PAVMs were not significantly different in the reperfusion group, compared to the non-reperfused group. Reperfusion was significantly associated with follow-up duration (\( p < 0.01 \)).

Patients were follow-up for a mean of 61.9 months (range, 7–168 months). Of the 13 patients, 6 underwent follow-up for more than 60 months (67–168 months; mean 113.8 months). One patient (case 5) temporally failed to attend follow-up sessions at five years, and another patient (case 7) was lost to follow-up, and was later admitted with acute stroke. Recanalization of embolized PAVMs was observed in 6 PAVMs (28.6\%) in 3 patients (23.1\%). One patient (case 5), in whom recanalization was detected 108 months after treatment, refused reembolization. In 1 patient (case 1) with four recanalized PAVMs 120 months after treatment, all recanalizations were associated with elongated and loosened microcoils. This patient demonstrated no recanalization 24 months after the second embolization (Fig. 1). In the third patient (case 7) with a giant mass-like PAVM treated with a detachable silicone balloon, recanalization occurred at 168 months (Fig. 2). He was admitted to our emergency room with acute stroke, and was found to have an acute thrombus in the right middle cerebral artery by cerebral angiography. Contrast-enhanced CT

Fig. 1. **G.** Chest radiograph obtained ten years after embolization shows elongated and loosened coils (arrows). **H.** Pulmonary angiogram obtained after repeat embolization of the 4r PAVMs shows complete obliteration of the feeding arteries (white arrows - complex type, black arrows - simple type).
scan demonstrated the presence of a collapsed silicon balloon and a thrombus-filled nidus. In addition, a small pulmonary vein was found to be attached to the nidus. This patient died due to complications related to infarction of the middle cerebral artery one month later. All 3 patients with recanalized PAVMs were identified during long-term follow up (mean, 132 months; range, 108–168 months).

**Discussion**

PAVMs are associated with hereditary hemorrhagic telangiectasia in 60–90% of cases [1–4], and conversely, approximately 15 to 35% of patients with HHT have PAVM [2–5]. However, patients with PAVMs in our study were not associated with HHT. PAVMs have been divided into simple and complex types according to their angioarchitectures. As described in previous studies, the simple type, with a smooth-walled aneurys-

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**Fig. 2.** A 55-year-old man with a mass-like PAVM.
A. Initial CT scan shows a mass-like PAVM in the right lower lobe. The detachable balloon has deflated in the feeding artery.
B. He is admitted to the emergency room due to acute stroke 168-months post-embolization. Cerebral angiogram shows the presence of an acute thrombus in the right middle cerebral artery.
C. A maximum intensity projection image of CT performed after admission shows the draining vein after recanalization (arrow).
D. A contrast-enhanced CT scan shows a thrombus-filled nidus in the previous-embolized PAVM (arrows).
mal sac, accounts for 80% of PAVMs, and the remainder are of the complex type, with septation or a more complicated relationship with multiple interconnecting vascular channels [1]. Furthermore, both types frequently co-exist. Approximately 53–70% of PAVMs are located in the lower lobes, while the remaining 35% are equally distributed among the lingual and the right middle lobe [3, 11, 12]. An extensive review of the pathologic anatomies in 350 patients with PAVM found that 75% had unilateral disease, 36% had multiple lesions, and half of the patients with multiple lesions had bilateral disease [11]. In terms of PAVMs in this study [B-12], the simple type (90%) appeared to be more common than in the Western population (80%) [3, 11, 12].

Symptoms related to PAVMs are more common in patients with HHT than in those without [13]. The presence of symptoms has been reported to be best correlated with lesion size [13]. Usually, a single PAVM of diameter < 2 cm is asymptomatic, symptoms occurred in 37% of patients with a single PAVM and in 59% of patients with bilateral PAVMs [13]. In the present study, 1 patient with PAVM-related symptom had a PAVN of 8 mm in diameter. Therefore, the incidence of PAVM-related symptoms in our Korean cohort was substantially lower than in Western populations [3, 11, 12].

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<th>Table 1. Patient and PAVM Characteristics Before and After Embolization</th>
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Note.—*: SP: subpleural, ^: S-simple: one feeder, C-complex: two feeders
`: Number of pulmonary arteriovenous malformations
RLL = right lower lobe, RML = right middle lobe, RUL = right upper lobe, LLL = left lower lobe

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<th>Table 2. PAVM Characteristics at Embolotherapy in Patients with Recanalized PAVMs</th>
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Note.— **PAVM** = pulmonary arteriovenous malformation
lower than has been reported in the Western populations [3, 11–14]. The most common presenting symptom was dyspnea on exertion, present in 31% to 67% of patients [12–14]. Furthermore, the majority of patients tolerated hypoxemia well and remained relatively or completely asymptomatic until arterial oxygen pressure fell below 60 mmHg.

The most commonly reported complications related to PAVMs affect the central nervous system, with an incidence ranges from 19% to 59% [3, 14, 15]. The mechanism responsible probably involves the presence of a paradoxical embolism across the PAVM. Hemoptyis and hemothorax are less commonly encountered, but are life-threatening. Hemoptyis may be caused by intrabronchial rupture of a PAVM or endobronchial telangiectasia, while hemothorax may result from rupture of a subpleural PAVM. In a study of 143 PAVM patients referred for embolotherapy, 11 (8%) had history of massive hemoptyis or hemothorax. In our study, 1 patient (8%) had massive hemoptyis associated with pulmonary parenchymal hemorrhage.

The treatment goals include prevention of hemorrhage, improvement of hypoxemia, and most importantly, prevention of complications associated with the local absence of a pulmonary capillary filter. Embolization therapy depends on the occlusion of arteries feeding PAVMs, and is commonly achieved using detachable balloons or metallic coils. Recently, several investigators (6, 16–21) have described the use of new embolic devices, such as, platinum coils, detachable coils, or Amplatzer vascular plugs. In the present study, the embolic materials used were a detachable gold valve latex balloon, stainless steel coils, or platinum coils. White et al. [3] reported that 3 of 76 patients experienced recanalization after coil embolotherapy. However, Remy-Jardin et al. [22] reported that of 64 PAVMs followed for a period of 2–21 years (average 9.74 years), 25% showed recanalization. In addition, Sagara et al. [23] reported high incidence (57%; 8/14) of recanalization among PAVMs embolized with steel coils.

In the present study, 21 PAVMs in 13 patients were embolized, and 6 (28.6%) PAVMs in 3 patients (23.1%) recanalized, as demonstrated by contrast-enhanced CT or chest radiography. In particular, all 3 patients were detected during long-term follow up (mean, 132 months; range, 108–168 months). Furthermore, in the present study, the rate of recanalization was substantially greater at 60 months (3/6, 50%).

Persistence or reperfusion of an apparently successful-ly embolized PAVM may occur in 1 or more of the following 4 ways; (a) recanalization of an embolized vessel, (b) growth of a missed or previously small accessory artery, (c) bronchial or other systemic artery collateral flow into the pulmonary artery beyond the level of the embolization, and (d) pulmonary artery-to-pulmonary artery collateral flow (10, 16, 23–25). Recanalization of embolized vessel is believed to occur due to coil elongation or inadequate number of coils. In our study, we considered that in 2 patients recanalization was attributable to coil elongation and/or inadequacy.

Autodeflation of a detachable balloon, accompanied or not accompanied by recanalization, and symptom recurrence in a recanalized case have been reported [26]. In the present study, we performed embolization using a detachable balloon in a patient with mass-like PAVM in 1992. During the follow-up period, despite deflation of the detachable balloon, no late migration occurred. However, follow-up contrast enhanced CT imaging 15 years later revealed a collapsed silicon balloon and a thrombus filled nidus, which was connected to a small pulmonary vein. Potentially serious complications have been reported to occur in 2.0–2.7% of patients during follow-up after PAVM embolization, and these complications included cerebral abscesses and strokes [3, 24]. In the present study, one patient that developed recanalization at 168 months experienced an acute stroke due to occlusion of the middle cerebral artery.

The limitations of this study are mainly associated with its small cohort and the retrospective design. Although PAVMs have been associated with HHT and lesions are relatively well detected, PAVMs are rare among the Korean population. All of the samples included in this study were identified within 15 years at two medical centers. In addition, not all patients underwent clinical or radiographical examination during follow-up. Two patients with recanalized PAVMs were lost to follow-up, and in 1 of these 2 patients, recanalization was detected after an acute stroke. Furthermore, we did not attempt to indentify factors associated with reperfusion, such as, bronchial or other systemic arterial collateral flows into the pulmonary artery, or pulmonary artery-to-pulmonary artery collateral flow.

In conclusion, PAVM is a rare condition in Korea, and the majority of patients with PAVMs are asymptomatic. Furthermore, PAVMs usually belong to the simple type and are located in the lower lobes and in the subpleural region. Embolotherapy with coils is highly effective in the treatment of PAVMs, and it should be noted that pa-
tients who undergo embolotherapy require careful surveillance. Therefore, optimal follow-up schedules should involve a combination of clinical assessment, physiologic testing, and radiological imaging. Patients should be followed for at least 10 years or throughout their lifetime.

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References

한국의 폐동정맥기형: 임상양상과 색전술의 장기 추적 결과

이재야1∙곽효성1,2∙진공용1,2∙한영민1,3∙노병석4

목적: 폐동정맥기형의 일반양상과 치료로서 색전술의 장기추적관찰 결과를 보기 위한 연구이다.

d대상과 방법: 폐동정맥기형으로 색전술을 시행 받은 13명의 환자를 대상으로 하였다. 4명은 남자, 9명은 여자였으며 평균 연령은 19-67세(평균 44세)였다. 저자들은 폐동정맥기형의 형태, 위치, 크기, 증상을 포함한 일반적인 양상을 분석하였다. 또한, 색전술 후 치료의 효과를 조사하고 혈중산소포화도의 변화를 분석하였다.

결과: 13명의 환자에서 총 21개의 폐동정맥기형이 혈관조영술로 확인되었다. 9명(69.2%)의 환자는 단순 폐동정맥기형이었고, 나머지 4명의 환자는 다발성 폐동정맥기형이었다. 21개의 폐동정맥기형 중 19개는 단일 폐동정맥기형이었으며 이 중 16개는 폐하엽에 위치하였고 17개는 늑막하부에 위치하였다. 폐동정맥기형의 재개통과 혈전의 이동 등으로 말미암아 중대뇌동맥영역의 급성 뇌경색이 발생하였다.

결론: 폐동정맥기형의 색전술은 환자 대부분에서 효과적인 치료 방법이나 장기간의 추적검사가 반드시 필요하다.