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INTERVENTIONAL RADIOLOGY

ORIGINAL ARTICLE

Selective arterial embolization of renal angiomyolipoma: comparing ethanol–lipiodol emulsion and polyvinyl alcohol particles as embolic agents

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PURPOSE

To examine the effectiveness and safety of two embolic agents, an ethanol–lipiodol emulsion and polyvinyl alcohol (PVA) particles, for selective arterial embolization (SAE) of renal angiomyolipoma (AML).

METHODS

Retrospectively, we reviewed the medical records and imaging data of renal AML patients who received SAE in our hospitals between July 2007 and January 2018. Among those eligible for analysis were patients with complete medical information, preoperative and postoperative contrast-enhanced computed tomography scans, and follow-up data. An ethanol–lipiodol emulsion was used to embolize 15 AMLs, and PVA particles were used to embolize 16 AMLs. We compared the tumor responses and adverse events between the two embolization-agent groups.

RESULTS

After embolization, no significant differences were observed in the shrinkage rates: 34.2% ± 3.4% for the ethanol–lipiodol emulsion group and 26.3% ± 3.0% for the PVA particles group ($P = 0.090$). Minor post-embolization complications were also similar between the groups, and there were no severe adverse events. The length of hospital stay after SAE was 2.5 ± 0.5 days for the ethanol–lipiodol emulsion group and 1.9 ± 0.5 days for the PVA particles group and was not significantly different ($P = 0.425$).

CONCLUSION

The results showed that SAE with ethanol–lipiodol emulsion or PVA particles was safe and efficient in decreasing tumor size and controlling renal AML hemorrhage.

KEYWORDS

Angiomyolipoma, embolization, ethanol, kidney, polyvinyl alcohol

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Renal angiomyolipoma (AML) is a benign renal neoplasm consisting of abnormal vasculature, smooth muscles, and adipose tissue that accounts for 2%–6% of all kidney tumors.[1] Pathologically, AML can be more accurately characterized as a perivascular epithelioid cell neoplasm.[2] Most AMLs occur sporadically, but some are related to a tuberous sclerosis complex.[3] The overall incidence of sporadic AMLs is 0.44% (0.60% in females and 0.28% in males).[4] The abnormal blood vessels in AMLs are fragile and vulnerable to rupture because fibrous tissue replaces smooth muscles, and they lack an internal elastic lamina.[5]

Selective arterial embolization (SAE) has proven to be a potent therapy for reducing tumor size and preventing AML bleeding.[6] Due to its minimal invasiveness and lower risk of serious complications compared to surgery, it has recently been increasingly applied as pre-

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ventive therapy for AML.[7] Embolization of AMLs has been conducted with various materials, such as polyvinyl alcohol (PVA) particles, microcoils, gelatin sponge, ethanol, and ethiodized oil (lipiodol). These are widely used to attain total embolization of the distal AML vascular bed. Ethanol is a liquid embolic agent that achieves permanent occlusion of the distal vascular bed and tumor tissue necrosis. The most dangerous complication associated with ethanol application is unspecified embolization caused by ethanol reflux from tumor-feeding vessels, which can lead to devastating consequences.[8,9] As one of the representative particulate embolic agents, PVA particles can also provide permanent occlusion, and there is extensive expertise in their use. Few previous studies have compared the efficacy or complications of different embolic materials used for renal AML embolization. This study aims to compare the efficacies, safety, and outcomes of two types of embolic agents utilized for SAE of renal AMLs: an ethanol–lipiodol emulsion and PVA particles.

Main points

- Selective arterial embolization (SAE) is a highly efficient therapy for reducing tumor size and preventing hemorrhages in renal angiomyolipoma (AML).
- Conducting SAE with the ethanol–lipiodol emulsion or polyvinyl alcohol (PVA) particles was a safe and efficient management option for reducing tumor size and controlling renal AML hemorrhages.
- The use of PVA particles as an embolic agent in SAE for renal AMLs can drastically reduce the tumor size and preserve renal function without imparting the high-risk and potentially devastating consequences associated with ethanol use.

Methods

Patient population

We retrospectively analyzed the medical information and imaging data of renal AML patients who received SAE at our hospitals between July 2007 and January 2018. Among the patients eligible for this study were those with complete medical information, preoperative and postoperative contrast-enhanced computed tomography (CT) scans, and follow-up data. Demographic information, clinical manifestations, tumor size and location, shrinkage rate, technical success, complications, hospital day after SAE, serum white blood cell count, and creatinine changes were recorded. The indications of SAE were acute hemorrhage, flank pain, and tumors greater than 4 cm in maximum axial diameter. Our work received ethical approval from the Institutional Review Board of the The Catholic University of Korea's Catholic Medical Center (approval number: 2021-0071-0001).

Angiography and embolization methods

An angiography was performed on the common femoral artery with the patient under local anesthesia. Abdominal aortography was conducted to identify the renal arteries and determine the presence of alternative feeding vessels. Selective renal artery catheterization and arteriography were performed via 5Fr angiographic catheters. When the target AML's feeding vessels were identified, a coaxial microcatheter was used to perform super-selective catheterization. Based on the size and quantity of the tumor-feeding vessels, a suitable amount of embolic material was carefully injected under continuous fluoroscopic guidance. Ethanol–lipiodol (Lipiodol® Ultra Fluid, Guerbet, France) emulsion and PVA particles (Contour®, Boston Scientific, USA) were chosen as embolic agents and used at the physician's discretion to occlude the AML vessels. Additionally, microcoils (Concerto®, Medtronic, USA; Tornado®, Cook Medical, USA) were used to treat aneurysms or to embolize AMLs' proximal feeding arteries when larger than 2 mm after distal embolic occlusion to avoid the possibility of incomplete occlusion of the feeding artery or recanalization. Tumor devascularization was confirmed by post-embolization arteriography.

Assessment methods

We examined both the medical information and associated images, along with the clinical success rate, technical success rate, and complications. Clinical success was defined as decreased target tumor size without severe complications attributable to SAE. Technical success was defined as complete tumor devascularization and lack of tumor staining in the target vessels. Tumor size was determined by measuring the maximum diameter on CT axial images. Moreover, the shrinkage rate was computed via a comparison of the maximum lesion diameter on the follow-up CT image with that on the initial CT image. Post-embolization syndrome (PES) was described as pain and fever after embolization treatment.

Statistical analysis

Continuous variables with normal distribution are expressed as means ± standard deviations (SD). Nominal variables are presented as counts and percentages. Student's t-test was employed for the comparison of continuous variables, and Fisher's exact test was used for the comparison of nominal variables. All data were analyzed using GraphPad Prism 6.01 software (GraphPad Software, San Diego, CA). A two-sided P value of <0.05 was set as the significance threshold.

Results

The demographic information is summarized in Table 1, and follow-up information is presented in Table 2, which includes a comparison of the different embolic agents used on the two groups. This study included 28 patients: 16 females (57.1%) and 12 males (42.9%) with complete medical records in the 11-year study period. The patients underwent 28 embolization procedures for 31 AMLs. The mean patient age at diagnosis was 49.3 ± 3.2 years. Six patients (21.4%) received SAE for hemorrhagic or symptomatic AMLs, whereas SAE was performed as a prophylactic therapy in 22 patients (78.6%). Regarding the location of the AMLs, 15 lesions (48.4%) were located in the right kidney and 16 (51.6%) were in the left kidney. There were multiple lesions in three patients (10.7%). Ethanol–lipiodol emulsion was used to embolize 15 AMLs, and PVA particles were used to embolize 16 AMLs. The mean follow-up duration was 11.5 ± 2.1 months for the ethanol–lipiodol emulsion group and 7.4 ± 1.4 months for the PVA particles group; however, the difference between them was not significant (P = 0.098).

The pre-embolization tumor size was 7.7 ± 0.7 cm in the SAE with ethanol–lipiodol emulsion group and 7.9 ± 0.6 cm in the PVA particles group (P = 0.809). The size decreases were comparable after SAE, as shown by the ethanol–lipiodol emulsion group's 34.2% ± 3.4% shrinkage rate (Figure 1) and the PVA particles group's 26.3% ± 3.0% shrinkage rate (Figure 2) (P = 0.090). With SAE, we achieved technical success in devascularizing the tumor-feeding arteries found on the angiographies of all patients. No patient in either group suffered serious complications after embolization. Furthermore, no patient experienced hemorrhagic complications from AMLs during the follow-up period. Therefore, all patients achieved clinical success. Seventeen patients (60.7%) experienced mild PES, which was resolved with conservative treatment only. Minor post-embolization complications were similar in both groups. The serum white blood cell counts of all patients before

and after SAE were 6.9 ± 0.5 (10^9/L) and 7.6 ± 0.5 (10^9/L), respectively. However, there was no significant difference (P = 0.172). In addition, the serum creatinine levels before and after SAE were all within the normal range. The length of hospital stay after SAE was 2.5 ± 0.5 days for the ethanol–lipiodol emulsion group and 1.9 ± 0.5 days for the PVA particles group, respectively, with no significant difference (P = 0.425).

Table 1. The demographic data

Variable	All patients (n = 28)	Ethanol–lipiodol emulsion (n = 12)	Polyvinyl alcohol particle (n = 16)	Statistical significance (P value)
Age (years)	49.3 ± 3.2	51.1 ± 4.5	47.9 ± 4.6	0.638
Gender				0.459
Male	12	4	8	
Female	16	8	8	
Masses				0.067
Single	25	9	16	
Multiple	3	3	0	
Location of tumor				1.000
Left	13	5	8	
Right	14	6	8	
Bilateral	1	1	0	
Aneurysm				1.000
Yes	2	1	1	
No	26	11	15	
Rupture				0.600
Yes	4	1	3	
No	24	11	13	

Table 2. Follow-up data and the comparison between the two groups of different embolic agents

Variable	All patients (n = 28)	Ethanol-lipiodol emulsion (n = 12)	Polyvinyl alcohol particle (n = 16)	Statistical significance (P value)
Follow-up periods (months)	9.1 ± 1.2	11.5 ± 2.1	7.4 ± 1.4	0.098
Tumor size (cm)				
Pre-embolization	7.8 ± 0.4	7.7 ± 0.7	7.9 ± 0.6	0.809
Post-embolization	5.5 ± 0.4	5.2 ± 0.6	5.8 ± 0.5	0.418
Decrease in size (cm)	2.3 ± 0.2	2.5 ± 0.2	2.1 ± 0.3	0.319
Shrinkage rate (%)	30.1 ± 2.3	34.2 ± 3.4	26.3 ± 3.0	0.090
Serum white blood cell counts (10^9/L)				
Pre-embolization	6.9 ± 0.5	7.0 ± 0.8	6.8 ± 0.6	0.822
Post-embolization	7.6 ± 0.5	7.0 ± 0.6	8.1 ± 0.8	0.310
Serum creatinine (mg/dL)				
Pre-embolization	0.7 ± 0.03	0.7 ± 0.03	0.8 ± 0.05	0.086
Post-embolization	0.8 ± 0.04	0.7 ± 0.04	0.8 ± 0.06	0.156
Post-embolization syndrome				0.253
Yes	17	9	8	
No	11	3	8	
Hospital days	2.0 ± 0.4	2.5 ± 0.5	1.9 ± 0.5	0.425

Discussion

Hemorrhaging caused by renal AMLs can be life-threatening, so it is common practice to treat patients who display symptoms or have tumors greater than 4 cm.[10] A previous study found that SAE of renal AMLs greater than 4 cm may reduce the risk of hemorrhaging.[11] The process of SAE has become a favorable management option for renal AMLs in both prophylactic and emergency cases for decades due to the recent technological advances in microcatheters and diagnostic imaging equipment. The current study demonstrates that the size of a renal AML decreases significantly after SAE, but renal function displays no obvious change. The present finding of a 30.1% ± 2.3% reduction in axial dimension is in accordance with previous reports,[12,13] which illustrates SAE's effectiveness in shrinking renal AMLs. Moreover, the present study's major finding concurs with the interpretation of a systematic review that reported a 93.3% average technical success rate with no procedure-related deaths and included 31 reports on 524 renal AML cases treated with SAE.[6] Nevertheless, these reports showed that among 263 AML patients with an average follow-up period of 39 months, there was an average 38.3% shrinkage rate after SAE, which is higher than that of the present study (mean ± standard deviation: 30.1% ± 2.3%). This discrepancy could be attributable to different radiological follow-up periods. The average follow-up duration of our study was only 9.1 months.

The ethanol–lipiodol emulsion and PVA particles in this study were successfully used as primary embolic agents for SAE. Ethanol is a liquid embolizing agent that permanently occludes arteries and capillaries at the distal level of collateral inflow and accelerates necrosis of tumor tissue. The primary risk of employing ethanol is unspecified embolization owing to reflux from tumor-feeding blood vessels, which can lead to devastating consequences.[8,9] Since ethanol is very destructive, SAE performed with ethanol sometimes presents serious problems in the embolization area. An ethanol injection into the proximal part of a tumor results in occlusion of the tumor's proximal blood vessels; however, viable tissue can remain in the distal tumor areas. Therefore, the decrease in tumor size may be inadequate and accompanied by an elevated risk of tumor recurrence.[14] Balloon-assisted SAE with ethanol for renal AML has been suggested[15] to avoid ethanol reflux and occlusion of both proximal arteries. However, the use of a balloon catheter may increase the aneurysmal rupture risk, which results from rising pressure during treatment and makes super-selective catheterization more difficult.[16]

Pulmonary complication is another risk of SAE performed using ethanol for renal AML

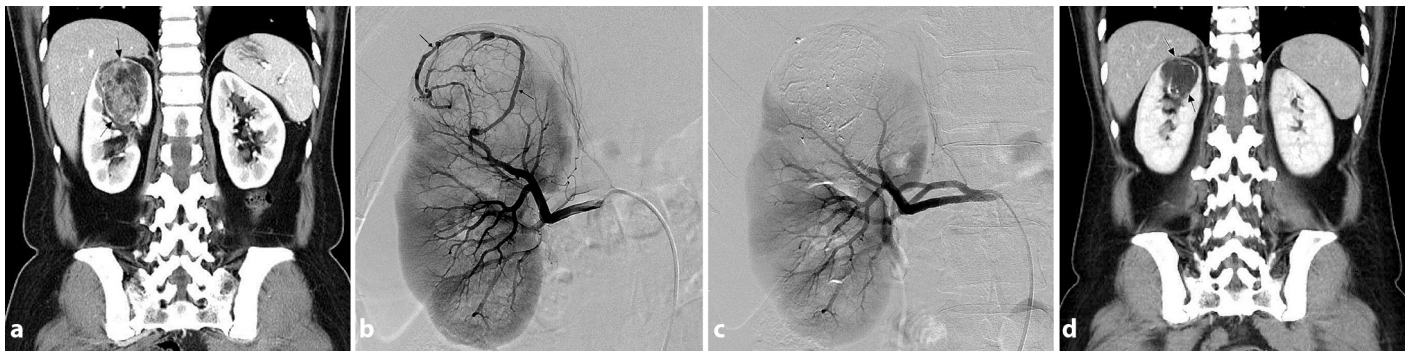

Figure 1. A 49-year-old woman presented with angiomyolipoma of the right kidney and underwent SAE with ethanol-lipiodol emulsion. **(a)** Pre-treatment CT showing a large tumor at the upper pole of the right kidney (arrows) composed of muscular, vascular, and fatty tissue. **(b)** Selective arteriography displaying a large hypervascular tumor with tortuous and disordered vessels (arrows). **(c)** Post-embolization arteriography showing complete occlusion of the vessels and no residual tumor staining. **(d)** A CT 13 months after embolization revealing significant shrinkage of the tumor (arrows). CT, computed tomography; SAE, selective arterial embolization.

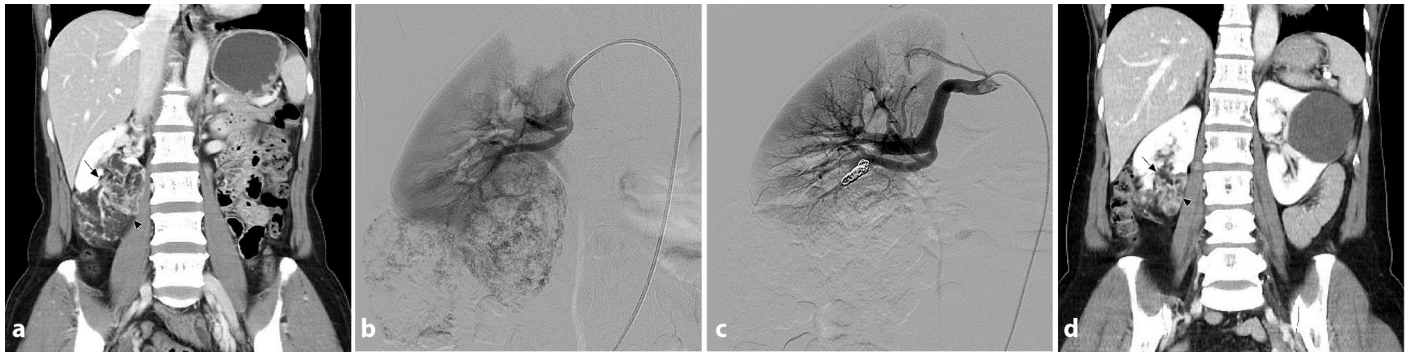

Figure 2. A 42-year-old woman presented with angiomyolipoma of the right kidney and underwent selective transarterial embolization with polyvinyl alcohol particles and microcoils. **(a)** A CT showing a large tumor with fatty content protruding from the right kidney (arrows). **(b)** Selective arteriography of the right renal artery displaying feeding branches and tumor staining. **(c)** Post-embolization arteriography showing the tumor staining's complete disappearance. **(d)** A CT seven months after embolization revealing a significant reduction in the size of the tumor (arrows). CT, computed tomography.

treatment. Pulmonary arterial pressure can accumulate during vascular malformation treatment when using ethanol.[17] Hiraki et al.[18] documented a patient with renal AMLs and lymphangioleiomyomatosis afflicted with pulmonary edema following transarterial embolization with ethanol. This patient's pulmonary edema led to the development of dyspnea and hemoptysis. In the latest study, although a micro-balloon catheter was employed to prevent ethanol reflux from injuring normal renal parenchyma, 42% of patients experienced renal parenchyma infarctions.[19] Therefore, ethanol must be employed with caution to prevent pulmonary and renal complications.

Particulate agents, such as PVA particles, are the most common type of embolic materials used for the treatment of renal AMLs and have been classified as permanent embolic agents.[20] With a size of 355–500 µm, PVA particles facilitate distal vascular occlusion of a tumor.[21] Particulate agents cannot be readily eliminated from target lesions following embolization, which leads to a prolonged delay in the recanalization of tumor-feeding vessels. Commonly, particulate embolization is done with a combination of 355–500 µm PVA particles, which block the target lesions' distal vascular bed. Then, coils are used to occlude the arterial inflow and halt retrograde filling of the aneurysm and reforming of abnormal tumor vessels.[22] The use of coils alone should be avoided because they only provide proximal blood vessel occlusion, which may cause collaterals around or at the distal level of the blockage and make embolization more difficult or impossible.[23,24] In the present study, nine patients underwent SAE with a combination of 150–350 µm PVA particles, six patients underwent SAE with a combination of 355–500 µm PVA particles, and one patient's SAE used 150–350 µm and 560–710 µm PVA particles. This study resulted in no obvious difference between the tumor shrinkage rates of the ethanol–lipiodol emulsion group and the PVA particles group and showed drastic reductions in tumor size post-SAE in both groups.

This study had two limitations: the retrospective design and the small sample population, which was due to AML being an uncommon benign tumor and a rare disease in our country. Studying a large sample may take a very long time. Another reason for the study's small sample size is that several patients with incomplete radiological follow-up data were excluded. Additionally, because of the low level of patient compliance during follow-up, the follow-up duration varied from 1–29 months with a mean of 9.1 months.

In summary, the study demonstrated that SAE with an ethanol–lipiodol emulsion or PVA particles was a safe and efficient management option for controlling hemorrhages and preventing renal AML progression. Using PVA particles as an embolic agent in SAE for renal AMLs can drastically reduce the tumor size and preserve renal function without imparting the high-risk and potentially devastating consequences associated with ethanol use. Prospective investigations of a substantial scale and with prolonged follow-up periods would be useful for identifying improved embolic agents for SAE of renal AMLs.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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