Safety, Efficacy, and Predictors for Late Reintervention After Embolization of Renal Angiomyolipomas – Embolization renaler Angiomyolipom

Sicherheit, Wirksamkeit und prädiktive Faktoren für eine späte Re-Intervention nach Embolisation von renalen Angiomyolipomen – Embolisation renaler Angiomyolipome

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ABSTRACT

Purpose To retrospectively analyze the procedural and long-term clinical outcome of the selective embolization of renal angiomyolipoma. In addition, potential predictive factors for higher risk of late re-intervention were analyzed.

Methods Retrospective monocentric study, including 34 consecutive patients, analyzing the safety, efficiency, and long-term clinical outcome of catheter-directed embolization of renal AML. Additionally, the difference in postembolization renal function between patients embolized in the acute and in the elective setting was analyzed. Secondly, we also evaluated whether volume/diameter of the AML and presence of intraleisonal aneurysms are risk factors for late re-intervention.

Results Embolization of renal AML was performed to control volume (n = 21; 62 %) or to stop spontaneous hemorrhage (n = 13; 38 %) with angiographic success in all cases but was associated with renal abscess (n = 1) and pulmonary embolism (n = 1) without a significant difference in renal function before and after embolization (P = 0.513). Volume/diameter (P = 0.276/P = 0.21) and presence of aneurysms before embolization (P = 0.37) are not predictive for a higher risk of late re-intervention.

Conclusion Catheter-directed embolization is a safe and effective treatment modality for asymptomatic and bleeding renal AML, without a negative impact on renal function. Initial mass volume/diameter or presence/absence of intraleisonal aneurysms does not seem to be predictive for late re-intervention.

Key Points:
• Complications related to renal angiomyolipoma embolization are rare.
• Embolization of angiomyolipoma will not reduce renal function.
• Initial volume or diameter of angiomyolipoma is not predictive for late re-intervention.

Citation Format
Introduction

Angiomyolipoma (AML) is the most common benign renal mesenchymal neoplasm containing smooth muscle, fat, and abnormal blood vessels in varying proportions [1, 2]. Because the blood vessels have no internal elastic lamina with replacement of the smooth muscle by fibrous tissue, they are fragile and prone to aneurysm formation or rupture [2, 3]. AMLs show a high likelihood of rupture during their clinical course, with the presentation of hematuria, retroperitoneal bleeding, and hemorrhagic shock [4].

AMLs are found in 0.3–5% of the general population and account for up to 3% of kidney masses [5]. Most AMLs (95%) are diagnosed based on the presence of macroscopic fat detected on computed tomography (CT), magnetic resonance imaging (MRI), and sometimes ultrasound. The majority of renal AMLs occur sporadically but they can also be associated with syndromes like tuberous sclerosis complex (TSC) or, less frequently, sporadic lymphangioleiomyomatosis (LAM) [6, 7].

Renal AMLs have the propensity to increase in size and may cause local complications including hemorrhage, mass effect, renal dysfunction, and venous thrombosis. Asymptomatic AMLs with a threshold diameter >4 cm or symptomatic AMLs for any tumor size are accepted indications for treatment [3, 7, 8].

Size of the tumor (diameter >4 cm), presence of intra-tumoral aneurysms, and presence of tuberous sclerosis are considered major risk factors for bleeding [3, 6, 8]. Therefore, AMLs smaller than 4 cm without intraläsional aneurysm are usually followed-up on a yearly basis, whereas it is recommended to treat AMLs larger than 4 cm to prevent hemorrhage [2, 3, 5]. While in the past imagensographic follow-up and targeted nephron-sparing surgery (NSS) or elective embolization were the only treatment options, patients with AMLs in the context of TSC or lymphangioleiomyomatosis (LAM) benefit from medicinal treatment with mammalian target of rapamycin (mTOR) inhibition. Multiple observations and randomized trials have shown considerable size-reducing effects of sirolimus and everolimus, with concurrent mitigation of bleeding risk without loss of functional renal tissue [9, 10].

The main goal of treatment is to reduce the risk of spontaneous hemorrhage and to ameliorate any other symptoms. Of the non-medicinal approaches, embolization is the preferred treatment because it is minimally invasive with a shorter recovery time and fewer procedure-related complications than NSS [2, 3, 7–9, 11–13]. Within the context of acute bleeding, arterial embolization is advocated as the first-line treatment [8]. Nowadays radical nephrectomy is only done in bail-out cases.

The objective of this study was to determine the safety and efficacy of catheter-directed embolization of renal AMLs. In particular, potential decrease in renal function of embolization was analyzed for patients embolized in elective versus urgent conditions. Second, we evaluated if there was a difference in recurrence rate after embolization between patients who were treated electively or in the acute setting.

Third, we evaluated if the initial presence of intraläsional aneurysms or larger volume/diameter of AMLs are associated with a higher rate of late re-intervention.

Materials and methods

1. Patients

This single-institution, retrospective study was approved by the institutional ethics committee. We included consecutive patients who underwent selective embolization of renal AMLs between
January 2000 and 2020. A total of 34 patients were included. Patients’ demographic, procedural, and follow-up data were collected from the patients’ electronic medical records and imaging data were retrieved from the Picture Archiving and Communicating System (PACS, Agfa Gevaert, Mortsel, Belgium). Volumetric analysis was performed on a dedicated workstation (Syngo.Via, Siemens, Forchheim, Germany) and AML vascularization score included:

1 = no visible aneurysm; 2 = one or more aneurysms > 5 mm diameter within the AML.

2. CT and MRI technique

The computed tomography (CT) protocol included a triple-phase scan: unenhanced, arterial, and venous, with the arterial and venous phases being 15 and 90 seconds after intravenous contrast injection, respectively (100cc Iomeron, Bracco, Milan, Italy). The technical parameters are: reference kV: 120, reference mAs: 180, rotation time: 0.5 s, pitch: 0.6, collimation: 128 × 0.6, slice thickness: 1 mm & 5 mm, slice increment: 0.5 mm & 5 mm and a soft tissue kernel.

The MRI protocol consists of a T2 haste coronal and transverse, T1 Dixon transverse in-opp bh 320, T1 vibe FS coronal and transverse, ep2 d diffusion, and post-contrast series transverse and coronal (T1 vibe in the corticomedullary phase, nephrogenic phase and the excretory phase) after intravenous injection of Gadoteric acid (Dotarem, Guerbet, Villepinte, France); the injected amount of contrast medium depends on the weight of the patient.

3. Angiographic and embolization technique

Angiographic embolization procedures were performed under local or general anesthesia related to the patient’s hemodynamic status. Percutaneous access was made to the common femoral artery ipsilateral to the affected kidney and a 4 or 5 French (F) vascular sheath was inserted. After abdominal flush aortography to identify the renal arteries, selective renal artery catheterization was performed with use of a 4 or 5 F Cobra catheter (Cobra Glidcath, Terumo, Leuven, Belgium or Cobra C2, Cook Medical, Bloomington, IN, USA) or Simmons I catheter (Glidcath, Terumo, Leuven, Belgium). Superselective catheterization of the angiomylipoma-feeding artery was performed with various types of microcatheters (Cantata 2.5, Cook Medical, Bloomington, IN, USA or Direxion 2.7, Boston Scientific, Natick, MA, USA or Progreat 2.4, Terumo, Leuven, Belgium). The embolization materials that were used included: tris-acryl gelatin microspheres (EmboSphere 300–500 μm, Merit Medical, South Jourdan, UT, USA), polyvinyl alcohol microspheres (Contour 150–255 μm, Boston Scientific, Natick, MA, USA), pushable microcoils (Target microcoils, Boston Scientific, Natick, MA, USA; microtornado, Cook Medical, Bloomington, IN, USA), detachable microplug (MVP, Medtronic, Minneapolis, MN, USA), or a glue mixture of Lipiodol (Guerbet, Villepinte, France) and enbucrylate (Histo-acryl, B. Braun, Melsungen, Germany) with a ratio 3/1. After embolization, completion renal angiography was performed, and the puncture site was manually compressed.

The angiographic endpoint included occlusion of all intralesional aneurysms in patients with an AML vascularization score of 2 or in occlusion of all AML arteries in patients with a sporadic AML with a vascularization score of 1.

4. Patients’ follow-up

Patients were followed-up clinically and by laboratory and imaging investigations including ultrasound, computed tomography, and magnetic resonance imaging. Imaging follow-up was performed yearly or every two years after embolization. The type of radiological follow-up study was at the discretion of the treating clinician and included ultrasound, CT, and MRI.

Indication for re-embolization included the identification of newly formed intrallesional aneurysms and/or growth of the AML mass lesion compared to the pre-embolization measurements or retroperitoneal hemorrhage.

5. Statistical analysis

A linear mixed model for repeated measurements was used to analyze change in kidney function between 3 timepoints, modelling a random intercept to deal with clustering by patient. Results are presented as mean differences with 95 % confidence intervals. The Mann Whitney U-test was used for testing a difference in kidney function and number of re-embolizations between patients with elective versus urgent embolization (change between pre-follow-up and follow-up). This test was also used for testing a difference in volume/diameter between patients with or without recurrence.

The Fisher exact test was used for testing a difference in recurrence between patients with a vascularization score of 1 versus 2/3.

Kaplan Meier estimates were used for overall survival.

Analyses have been performed using SAS software (version 9.4 of the SAS System for Windows, Cary, NY, USA).

Results

1. Patients’ demographics

The majority of included patients were women with a mean age of 51 years. 9 patients had an associated syndrome, and 13 patients were urgently treated for spontaneous retroperitoneal hemorrhage as summarized in Table 1. Five patients (15 %), all suffering from TSC, underwent everolimus medical treatment (Votubia, Novartis, Barcelona, Spain) for AML before referral to interventional radiology for embolization.

2. Procedural outcome results

The majority of patients (n = 22; 64.7 %) received a CT scan prior to the embolization procedure and were embolized with microparticles in combination with microcoils. One or more intrallesional aneurysms with a diameter > 5 mm were found in 15 patients (44.1 %) as summarized in Table 2. In all included patients, all intrallesional aneurysms were excluded by embolization. In patients with sporadic AML without intrallesional aneurysm, > 90 % of AML arteries were occluded. Procedure-related complications included renal, postembolization abscess (n = 1) (Fig. 1) and pulmonary embolism (n = 1). Both complications were successfully treated by medicinal (antibiotics and heparin, respectively) management. Mild to moderate embolization-related abdominal discomfort was noted in all patients and was managed with non-steroidal anti-inflammatory drugs.
3. Short- and long-term clinical outcome

All patients embolized for spontaneous retroperitoneal hemorrhage (n = 13; 38.2 %) recovered completely with a normalization of the hemoglobin level 1 month after the procedure. Renal function at 3 days post-embolization demonstrated a mean & median glomerular filtration rate of 82.2 and 83 ml/min/1.73 m², respectively. At 3 months of follow-up, the mean and median glomerular filtration rate was 80.3 and 85 ml/min/1.73 m² respectively. In addition, the glomerular filtration rate prior to versus three months after the procedure or three days versus three months after the procedure did not show any difference between patients who underwent a preventive versus urgent embolization procedure.

During follow-up, various imaging techniques were used to monitor the embolized AML: ultrasound was performed in n = 28 patients, CT and MRI were performed in n = 19 and n = 5 patients, respectively. Late re-embolization was performed in 6 out of 34 patients (17.6 %). The initial embolization in these 6 re-embolized patients was performed for retroperitoneal bleeding (n = 3) and as a preventive embolization (n = 3). In these 6 re-embolized patients, the indication for the second embolization was: re-bleeding related to newly formed aneurysms in the embolized AML (n = 3), re-bleeding related to newly formed aneurysms in the AML of the contralateral kidney (n = 2), and increase in AML volume (n = 1) without difference in risk for re-embolization between patients initially embolized for hemorrhagic and preventive indication (P = 0.557). In particular, in the 4 patients who underwent a second embolization, the indication for the re-embolization was retroperitoneal bleeding (n = 2) and preventive (n = 2). In the one patient who underwent 4 embolization procedures, the indication for re-embolization was retroperitoneal bleeding in all events, and in the one patient who underwent 7 embolization sessions, the indication for all 6 re-embolization sessions was retroperitoneal bleeding. The patient who underwent 3 re-embolization procedures, firmly asked for radical nephrectomy 12 months after the last embolization session.

Six out of 34 patients (17.6 %) died during the follow-up period; none of the deaths were documented as related to the AML or to the embolization procedure: three patients died related to non-renal neoplastic disease, including breast carcinoma (n = 1), colon carcinoma (n = 1), and endometrial carcinoma (n = 1); one patient died related to a bleeding liver adenoma and in two patients the cause of death was unknown, resulting in an overall estimated survival of 87.3 % and 69.5 % after 5 and 10 years of follow-up, respectively (Fig. 2).

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A 26-year-old woman with underlying sporadic lymphangioleiomyomatosis presents with an asymptomatic AML with a diameter of 8 cm in the left kidney. A. selective left renal angiography reveals the aberrant vascularity of the AML (arrows). B. Completion angiography after selective microparticle and microcoil (arrow) embolization shows complete devascularization of the AML. C. CT scan 14 days after embolization shows the devascularized AML (arrows) and small air bubbles (white arrowheads) within the AML, suggestive for abscess formation within the embolized AML.

Fig. 2 Kaplan-Meier survival curve shows an estimated survival of 87% and 69.5% after 5 and 10 years of follow-up, respectively.
4. Factors predicting late re-intervention

The initial vascularization score, volume, and maximal diameter of AMLs were analyzed for potential risk of late re-intervention. In total, 15 patients (44.1%) presented with one or more intralesional aneurysms on the initial selective renal angiography. The mean volume and mean maximal diameter of the AML were 209.9 cm³ and 68.9 mm, respectively. However, the presence or absence of intralesional aneurysms, total volume, or maximal diameter of the AML was not predictive for late re-intervention (P = 0.37; P = 0.276; P = 0.21 respectively).

Discussion

This study confirms the safety of catheter-directed selective embolization of renal AMLs in both the elective and the emergency setting with the use of mainly a combination of tris-acryl gelatin microspheres and microcoils, which is in line with other studies using the same combination of embolics [1, 14, 15]. Lenton et al. advocated the combined use of microparticles and coils as microparticles alone may predispose to acute hemorrhage during or soon after embolization. In their series, this complication was seen in 40% and 23% of acute and elective procedures, respectively [15]. This particular complication was not seen in the presented series mainly using a combination of microspheres distally and microcoils proximally to the AML-feeding vessels. As an alternative to the combined use of microspheres distally and microcoils proximally, glue as a mixture of cyanoacrylate and Lipiodol, as we used in 2 patients, or ethylene vinyl alcohol copolymer (Onyx) may be safely used in AML embolization procedures [12, 16]. The only serious complication encountered in the presented series was a postembolization renal abscess which was managed with intravenous antibiotic therapy and surgical drainage. Post-embolization renal abscess in AML may rarely occur with an incidence of less than 5% of cases [13, 14, 17]. Other rare and serious complications include pleural effusion, main renal artery thrombosis, and urinary tract infection [13, 18]. In this study, a transient, slight non-significant decrease in renal function 3 days after embolization with normalized values compared to baseline at 3 months after embolization was identified, which is in line with a meta-analysis by Lin et al. [19] demonstrating normalization of renal function at a mean of 6 months after index embolization. Baba et al. demonstrated that transcatheter embolization may not induce renal function on the embolized kidney by using 99m technetium-mercaptoacetyltriglycine 3 renography [20]. In addition, in the presented study, no differences in renal function change could be found in patients embolized in urgent versus in elective setting.

The relatively high re-intervention rate during follow-up seems to be the Achilles’ heel after AML embolization. In the presented study 6 patients (17.6%) needed at least one re-intervention. The indication for the second embolization was re-bleeding in the embolized AML (n = 3), bleeding in the contralateral kidney (n = 2), and increase in the AML volume (n = 1) which is in line with other studies [17, 21]. This number is lower than the re-embolization rate of 41.1% in the series by Anis et al. [13]. However, the median follow-up period in their study was more than 10 years and the median tumor size at baseline was nearly 9 cm compared to 6.9 cm in the presented study. Adversely, Lee et al. reported a very low re-embolization rate (4 out of 113 patients). These authors mainly used ethanol in combination with other embolics like Lipiodol to embolize AML [22].

In this study, we could not identify risk factors for late re-intervention. The presence of intralesional aneurysms or the maximum diameter/volume of the AML does not seem to be a good predictor for late re-intervention. In addition, re-interventions were performed both in the patient group prophylactically embolized and in the patient group embolized for retroperitoneal hemorrhage. Continuous clinical and radiological follow-up seems to be mandatory for all embolized patients irrespective of the composition and dimensions of the AML at baseline. As the majority of patients embolized for AML are relatively young and annual or bi-annual radiological follow-up seems to be required, MRI rather than CT is the radiological technique of choice [5].

Finally, there are multiple limitations of this study: first the retrospective nature of the analysis may bias the results; second, both pre-interventional as well as post-interventional imaging follow-up was not consistent with regard to the radiological technique and the time interval between two studies; third, different types of embolics were used, however, in the large majority of included cases, microspheres in combination with microcoils were used; fourth, clinical presentation (asymptomatic versus bleeding patients; sporadic versus TSC) was different among included patients and last, the number of included patients (n = 34) was small to draw robust statistical conclusions.

Conclusion

In conclusion, this retrospective study demonstrates that transcatheter embolization of renal AMLs is safe and efficient with unchanged postprocedural renal function in patients embolized in the urgent and in the elective setting. The reintervention rate was 27% and was related to rebleeding, continued growth of the embolized AML, or newly formed intralesional aneurysms, requiring continued radiological follow-up, preferentially by MRI.

Clinical relevance of the study

This study demonstrates the safety of selective embolization of renal angiomyolipoma using primarily microparticles. In addition, embolization was not associated with a decline in renal function. Last, the volume or diameter of the angiomyolipoma and the presence of intralesional aneurysms are not predictive for a higher risk of late re-intervention.

Conflict of Interest

The authors declare that they have no conflict of interest.

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