Renal Artery Embolization for Neoplastic Conditions

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Renal artery embolization (RAE) is a versatile tool for the management of both acute renal hemorrhage and nonemergent renal conditions. Acute bleeds may be encountered in the setting of trauma, iatrogenic injury, renal tumors, or aneurysms. Since its development in the 1970s–1980s, the use of RAE for acute hemorrhage has been shown to be both safe and efficacious, with reported success rates between 85 and 95%.^{1–3} Improvements in technology such as the coaxial catheter system have allowed for the use of superselective embolization, which minimizes the risk of irreversible renal function loss. With superselective technique, the infarcted portion of the kidney is typically less than 15%, and there is often no significant loss of renal function.⁴ For this reason, along with fewer complications and more rapid recovery compared with surgical management, RAE is considered the treatment of choice for acute renal hemorrhage when possible.^{5,6}

RAE can also be performed for a wide variety of non-emergent renal conditions. Patients with end-stage renal disease and consequent drug-resistant hypertension may be appropriate for RAE as a means of functional exclusion of the kidney, particularly those who are poor surgical candidates. For this indication, proximal embolization is performed with the goal of achieving complete necrosis of the kidney. This obviates the need to perform open or laparoscopic nephrectomy, which otherwise carries significant morbidity and mortality.^{7,8} Similarly, functional exclusion with RAE can be used to treat nephrotic syndrome and cases of graft intolerance syndrome associated with failed renal transplants.^{9–11} Less frequent indications include arteriovenous malformations, renal artery aneurysms, and autosomal dominant polycystic kidney disease. Benign and malignant neoplasms together comprise the most common indications for RAE, which will be reviewed in detail in this article.

Technical Considerations

Preprocedural planning with computed tomography angiography (CTA) or magnetic resonance imaging (MRI) is helpful to localize the lesion of interest, as well as identify the renal artery pattern and variant anatomy, such as an accessory or

polar artery. Proper planning can decrease procedure time, resulting in lower contrast and radiation dose for the patient, and less blood loss in cases of trauma. It is important to note, however, that small branches may not be readily seen on cross-sectional imaging, and particular attention should be paid on angiography to look for these.

Baseline laboratories including serum creatinine and international normalized ratio (INR) should be obtained prior to performing RAE. Preservation of renal function is often of special concern with this patient population. For those with low creatinine clearance, the risks and benefits of the procedure need to be weighed before proceeding. A nonionic isotonic contrast agent should be used to minimize the risk of kidney damage, though in select cases CO₂ angiography may be utilized. INR should be corrected to less than 1.5 and platelets transfused if less than 50,000. Society of Interventional Radiology (SIR) standards of practice guidelines recommend routine use of antibiotic prophylaxis, such as 1 g ceftriaxone given intravenously.¹² Moderate sedation and local anesthesia is sufficient in most circumstances.

RAE procedures are typically performed via femoral access with a micropuncture kit and placement of a short 5-Fr sheath. A flush catheter is advanced just above the renal arteries, at the T11 or T12 level, and an aortography is then obtained. The target renal artery can then be selected using a catheter such as a Cobra, SOS, or Simmons, and a renal angiography performed. Embolization can be performed just distal to the main renal artery ostium when complete necrosis is desired, or within a segmental or more distal branch using a microcatheter system when preservation of normal renal parenchyma is the goal.

A variety of embolic agents are available for use with RAE, though the material chosen should be tailored to the indication and goal of therapy. Polyvinyl alcohol particles, trisacrylgelatin microspheres, microcoils, N-butyl-2-cyanoacrylate glue, and ethanol diluted with iodized oil are all options for distal embolization, in both selective and nonselective fashion. When using particles and liquid agents, care should be taken to prevent reflux or nontarget embolization in the presence of an arteriovenous fistula. Coils are typically used for proximal embolization, with or without the addition of gelatin sponge.

Gelatin sponge alone may be used in select cases when the temporary embolic effect is all that is required.

Case Presentation 1

A 39-year-old woman with history of tuberous sclerosis was referred to urology to discuss an enlarging right renal angiomyolipoma (AML). Under serial surveillance, it had been progressively increasing in size and on most recent MRI measured $18 \times 17 \times 11$ cm. Interventional radiology was consulted for embolization (► **Fig. 1**).

Following preprocedural workup, the patient was brought to the angiography suite. Using a 5-Fr micropuncture system, the right common femoral artery was accessed. A J-wire was advanced into the aorta and a 5-Fr sheath was placed. Next, a 5-Fr pigtail catheter was used to perform a flush aortography. This was exchanged for an RC1 catheter.

The right renal artery was selected and angiography was performed. A dominant feeding branch arising from the lower pole of the right kidney was identified supplying the large AML, without evidence of shunting. A microcatheter was advanced to the distal segment of the feeding vessel and embolization was performed using 500 to 700 μ m Embospheres (Merit Medical, South Jordan, UT) until near stasis was achieved. The main feeding artery branch was then embolized using two 3-mm pushable coils.

Postembolization angiography demonstrated no flow beyond the coil pack, with sparing of the remaining renal vessels. The catheters were removed. Right common femoral artery angiography was performed through the sheath demonstrating a patent right common femoral artery. Angio-seal closure device (Terumo Corporation, Tokyo, Japan) was used to achieve hemostasis. The patient tolerated the procedure without immediate complication. Follow-up MRI showed a significant decrease in size of the mass, measuring $13 \times 13 \times 9$ cm.

Angiomyolipoma

Renal AML is a type of hamartoma composed of fat, smooth muscle, and thick-walled blood vessels.¹³ They can occur sporadically or in association with tuberous sclerosis complex (TSC) or lymphangiomyomatosis (LAM). AMLs demonstrate a variable rate of growth throughout life and pose a risk

of rupture when large enough.¹⁴ Detection of an AML may occur incidentally on imaging for another indication, through screening in a patient with TSC, or in the symptomatic patient after rupture.

Ruptured AMLs may be contained to a small perinephric hematoma or result in a life-threatening retroperitoneal bleed. Patients present with flank pain, a palpable mass, gross hematuria, and sometimes shock. Conservative surgical management in the setting of a ruptured AML is challenging, and often results in complete nephrectomy.¹⁴ In contrast, RAE can be used to selectively target the bleeding AML, preserving the nonaffected parenchyma. Currently, RAE is considered first-line treatment for ruptured AML, with surgery limited to use when RAE is technically infeasible or unavailable. Several embolic agents have been used.^{15–17} One commonly described method involves distal embolization of the tumor bed with an agent such as ethanol mixed with iodized oil, combined with coiling to treat microaneurysms if present. The need for surgical management following RAE for bleeding AMLs is rare, and the relatively few instances of rebleeding are often successfully treated with reembolization.^{15,17–19}

There is no consensus on the exact circumstances for which an asymptomatic AML should be treated prophylactically. Increasing tumor size is a known risk factor for rupture, and a size greater than 4 cm is often cited as the lowest threshold for intervention.^{13,20,21} Other factors may contribute to the decision to treat prophylactically. AMLs in patients with TSC tend to be faster growing and more likely to rupture.²² These patients are often aware of AML growth based on surveillance imaging, and a discussion of the benefits of embolization should be initiated when tumor size approaches 4 cm. Pregnancy is also associated with increased potential for rupture.²³ Patients with a known AML who plan to become pregnant should be counseled on the risk and offered prophylactic treatment if the tumor is large enough. The presence of a microaneurysm larger than 5 mm in size has also been suggested to increase risk of bleeding and may factor into the timing of intervention.²⁴ For those at lower risk for rupture, surveillance with periodic imaging is recommended. Medical management with an mTOR inhibitor such as sirolimus has been used for patients with TSC, with significant reduction in AML size demonstrated; however, the benefit is questionable

Fig. 1 A 39-year-old woman with tuberous sclerosis with enlarging right renal mass. (a) Coronal T2-weighted image demonstrating a large exophytic angiomyolipoma (AML) arising from the inferior pole of the right kidney (arrow). (b) Selective right renal artery angiography showing a single feeding artery supplying the large lower pole AML with typical vascular appearance. (c) Postembolization right renal artery angiography demonstrating cessation of flow to the feeding artery, with sparing of the remainder of the kidney. (d) Coronal T2-weighted image from MRI obtained 6 months following embolization shows a significant decrease in size of the right lower pole AML (arrow).

in consideration of the significant side effect profile associated with these medications and uncertainty whether reduction in size truly reduces risk of bleeding.²⁵

Follow-up imaging after embolization of an AML is often obtained within the first 6 months to evaluate treatment response, and is variable thereafter. Reduction in size of the AML is typical but not always seen. One study that describes 39 cases of embolized AMLs identified a mean tumor volume reduction of 72%, and further showed that reduction in size was greater in tumors with less fat content.²⁶ Currently, there is no consensus on long-term surveillance of an AML following RAE; however, data suggest it may be unnecessary for cases of sporadic AML. Two studies that followed up patients for a mean time of 4.3 and 4.8 years found recurrence rates of 31.6 and 37%, respectively.^{15,17} In one of these studies, all recurrences were in TSC patients, and in the other there was a trend toward statistical significance for the association of TSC and recurrence. Most recommend a surveillance frequency of every 1 to 2 years to follow up at risk AMLs in patients with TSC.

Case Presentation 2

A 58-year-old man was transferred to our medical center to be seen by urologist after presenting at an outside hospital with chest and abdominal pain. CT pulmonary angiography was performed and demonstrated a 10 × 12 cm hypervascular mass originating from the left kidney, highly suspicious for renal cell carcinoma (RCC). Urology determined the large size of the lesion, and findings of tumor abutting the pancreas, parasitic vessels, and renal vein invasion to the IVC were prohibitive for laparoscopic resection. Interventional radiology consultation was sought for preoperative RAE with a goal of tumor debulking and reduction in intraoperative blood loss (→Fig. 2).

Following a preprocedural workup, the patient was brought to the angiography suite. Using a 5-Fr micropuncture system, the right common femoral artery was accessed, and a 5-Fr sheath was placed. Next, a 5-Fr pigtail catheter was advanced to the abdominal aorta. An aortography demonstrated a large

hypervascular tumor arising from the left kidney. The left renal artery was selected, and three separate second-order vessels supplying the mass were identified. Each of these vessels was embolized with multiple microcoils. A postembolization angiography demonstrated adequate stasis of all distal vessels. Repeat aortography demonstrated a patent renal artery proximal to the embolized segments, with normal flow to the remainder of the kidney.

The patient tolerated the procedure well without immediate complication. The patient was taken the following day for uncomplicated nephrectomy. Pathology confirmed RCC, clear cell type.

Renal Malignancies

In contrast to AML, surgery remains the first-line treatment for renal malignancies in appropriate candidates. Depending on both patient and tumor characteristics, radical or partial nephrectomy may be performed with an open, laparoscopic, or robotic approach. More recently, ablative therapies such as radiofrequency ablation (RFA) and cryoablation are being used for small, peripherally located tumors in patients who are poor surgical candidates. RAE is not typically used as a primary treatment of renal malignancies, but does have a supportive role in select cases.

The risk of large intraoperative blood loss during resection of a hypervascular tumor such as RCC is the basis for a type of preoperative embolization sometimes employed prior to nephrectomy.²⁷ This is one of the earliest applications of RAE, and the most common indication pertaining to renal malignancies. Several other benefits are also attributed to the procedure.^{28,29} Following RAE, the development of edema surrounding the infarcted kidney is believed to make cleavage easier during the surgery. Another advantage during surgery is the ability to ligate the renal vein prior to the renal artery, which is helpful during resection of tumors involving the hilum or when there is significant adenopathy.²⁹ A few studies showed that tumor necrosis following RAE was associated with an increased tumor-specific immune response, which would be beneficial in the presence of metastases; however, there has been little data to support this subsequently.^{30,31}

Fig. 2 A 58-year-old man with chest and abdominal pain. (a) Coronal contrast-enhanced CT with findings of a large left renal mass consistent with renal cell carcinoma (arrow). (b) Selective left renal artery angiogram demonstrating supply to the hypervascular left renal mass. (c) Following coil embolization of three second-order arteries, a selective left renal artery angiography shows adequate stasis of flow.

Finally, RAE may reduce tumor thrombus burden prior to surgery.

As with other indications for RAE, preoperative embolization of renal cancer can be performed using several different embolic agents, often a combination of two or more. Gelatin sponge can theoretically be used as a single agent, as the temporary embolization effect is sufficient when a short interval to surgery is expected. When partial nephrectomy is planned, embolization is performed in a selective or superselective manner to minimize necrosis of the future remnant kidney. If radical nephrectomy is planned, proximal embolization is additionally performed, typically with use of coils. The optimal timing for RAE in these cases is generally accepted to be between 24 and 72 hours prior to planned surgery.²⁸ This allows local edema to develop, but limits formation of collaterals and symptoms of postembolization syndrome (PES).

Despite decades of use, there is a lack of prospective data supporting RAE prior to nephrectomy. One retrospective study comparing 118 patients with RCC who underwent preoperative RAE to matched controls who were treated with nephrectomy alone found a benefit to the procedure, with 5-year survival rates of 62 and 35%, respectively.³² A more recent retrospective study of 378 total matched patients found no statistically significant difference in 5-year cancer-specific survival or overall survival when RAE was used prior to nephrectomy.³³ Other measures such as operative blood loss and duration of surgery have similarly shown mixed results.^{28,34,35} A recent small case series demonstrated a new approach to zero ischemia partial nephrectomy with the use of a hybrid operating room for same-day preoperative RAE and surgery.³⁶ The role of preoperative RAE may be further defined, as variations on technique such as this are explored.

In addition to its preoperative role with nephrectomies, RAE is also occasionally used as an adjunctive therapy for patients with small renal cancers treated with percutaneous ablation. Selection criteria for the use of ablation and the considerations specific to the different types of probes used is beyond the scope of this article, but in general its use can be described as appropriate for patients with small tumors when surgical risk is prohibitive or more conservative management is desired. The use of adjunctive RAE with RFA was first described in 2000 by Hall et al.³⁷ Since that time, several case reports and studies have demonstrated the technique to be technically feasible and safe.^{38,39} The purported benefits of combining RAE with ablation include reduction of postablation hemorrhage, increased tumor visualization on CT guidance when lipiodol-containing agents are used, reduced heat-sink effect with RFA technique, and cost-savings associated with decreased number of probes required following tumor shrinkage.^{40–42} Currently, there is no consensus or hypothesis on the optimal timing of RAE prior to ablation. Some of the larger case series in the literature have reported an interval between 6 and 10 days prior to ablation; however, this is more variable than when used as an adjunct for nephrectomy.^{42,43}

For large unresectable renal malignancies, and in those with metastatic disease, RAE may be performed for palliative purposes. The procedure has been shown to be beneficial for palliation of tumor-related bulk symptoms and recurrent

hematuria.⁴⁴ While marginal survival benefit has been demonstrated with cytoreductive nephrectomy in patients with metastatic disease, there is currently no data comparing cytoreductive nephrectomy to RAE in this setting, and therefore its use is typically reserved for patients who have a need for symptomatic relief.

A recently published prospective randomized study by Karalli et al evaluated the cytoreductive effect of bland RAE to chemoembolization in patients with RCC using drug-eluting particles prior to nephron-sparing or radical nephrectomy in 11 patients.⁴⁵ Chemoembolization was shown to result in necrosis of 88.3 and 87.5% on average by CT and histopathologic evaluation, respectively, compared with 29.4 and 26% for bland embolization. While all patients irrespective of treatment group were shown to have residual viable tumor cells by microscopy, the significant increase in cytoreductive effect seen in the chemoembolization group may indicate a role for this technique in the future for the palliative treatment of unresectable or metastatic renal cancer.

Complications

The overall complication rate for RAE is low. Most technical complications, including access site hematoma, arterial dissection, and contrast-induced nephropathy, are not specific to the procedure. The risk of nontarget embolization had been reduced significantly with improvements in technology since the procedure was first pioneered. Coil migration, a potentially serious complication, has a reported incidence of 2%,⁴⁶ though this may be lower now as the use of liquid and particle embolic agents has increased.

As with other embolization procedures that cause necrosis, PES is frequently encountered after RAE, characterized by fever, nausea, leukocytosis, and flank pain. PES may occur in up to 90% of patients who undergo RAE, and is more common with nonselective embolization.⁴⁷ One small case series found a significant decrease in the rate of PES when a course of steroids was given to the patients while RAE was performed⁴⁸; however, this is not currently a standard of care. Supportive treatment with antiemetics and analgesics is often sufficient for the treatment of PES, and symptoms typically resolve within 2 to 3 days.

Conflict of Interest

T.G.V.H.: Cook Inc., Site PI research grant.

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