Trans-Arterial Embolization of Renal Cell Carcinoma prior to Percutaneous Ablation: Technical Aspects, Institutional Experience, and Brief Review of the Literature

Andrew J. Gunn a Benjamin J. Mullenbach b May M. Poundstone a Jennifer B. Gordetsky c Edgar S. Underwood a Soroush Rais-Bahrami d

a Division of Vascular and Interventional Radiology, Department of Radiology; Department of b Radiology, c Pathology, and d Urology, University of Alabama at Birmingham, Birmingham, AL, USA

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Abstract
This report describes the technical aspects of trans-arterial embolization (TAE) of renal cell carcinoma prior to percutaneous ablation. All patients (n = 11) had a single renal mass (mean tumor diameter = 50.2 mm; range: 28–84 mm). Selective TAE was performed via the common femoral artery. Embolic materials included: particles alone (n = 4), coils alone (n = 1), particles + ethiodized oil (n = 2), particles + coils (n = 1), ethiodized oil + ethanol (n = 2), and particles + ethanol (n = 1). All embolizations were technically successful and no complications have been reported. After embolization, 10 patients underwent cryoablation while 1 patient underwent microwave ablation. Ablations were technically successful in 10 of the 11 patients. Only 3 minor complications were identified but none required treatment. No adverse effect on the patient’s glomerular filtration rate was seen from the additional procedure (p = 0.84). TAE of renal cell carcinoma prior to percutaneous ablation is safe and technically-feasible.

Introduction
Renal cell carcinoma (RCC) accounts for approximately 4% of all cancer cases in the United States [1]. Its incidence, however, is increasing secondary to the identification of renal tumors in patients who are imaged for other reasons [2–5]. One unintentional benefit of these incidentally-detected renal masses is that they are typically smaller, of lower grade, and have been associated with longer disease-free survival [6]. Given this smaller size, less invasive treatment options such as partial nephrectomy, laparoscopic ablation, and percutaneous ablation are being used as safe and effective alternatives to radical nephrectomy [6–12]. Yet, many patients are not optimal operative candidates or may wish to avoid traditional surgery, thus percutaneous ablation offers patients a non-surgical, minimally-invasive option with similar outcomes to partial nephrectomy in T1a RCC [13]. The outcomes and complications associated with percutaneous ablation in RCC are dependent on tumor size, geometry, and vascularity [14, 15]. Since RCC is a highly vascular tumor, bleeding is one of the major complications seen after percutaneous ablation [16]. Nonetheless, the vascularity of RCC could potentially provide an intriguing target for adjunctive therapy...
as several reports in the literature describe trans-arterial embolization (TAE) of RCC prior to percutaneous ablation as a means to improve tumor localization, increase tumor ischemia, and decrease post-procedural bleeding [17–24]. Therefore, the purpose of this manuscript is to provide practitioners a guide to the technical aspects of these procedures, discuss our institutional outcomes, and provide a brief review of the literature so that they may best determine which patients could benefit from this treatment approach.

**Technical Aspects**

**Patient Selection**

A multi-disciplinary clinic would be an optimal location for the patient to receive concurrent consultation from a urologic oncologist and interventional radiologist. Yet, patients are typically referred from urology to interventional radiology (IR) for evaluation of potential percutaneous renal tumor ablation. Once referred, the patient should ideally have a consultation with the treating IR where the risks, benefits, and alternatives can be explained in detail. This also provides an opportunity to thoroughly review the pre-procedural imaging. Special attention should be paid to the presence of any additional renal masses, supernumerary renal arteries, renal atherosclerotic disease, abdominal aortic aneurysms, or peripheral vascular disease that may make TAE more challenging. Moreover, a safe percutaneous route for the ablation that avoids damaging normal structures such as the renal pelvis, ureter, inferior vena cava, aorta, and adjacent bowel should be identified. While many of these obstacles can be overcome to safely perform both TAE and percutaneous ablation, it is advisable to develop a plan prior to the date of the procedure and make the patient aware of what case specific difficulties may arise. The patient’s laboratory results are reviewed with particular attention to the platelets (should be > 50 × 10^9 / µl), international normalized ratio (should be < 1.5), and glomerular filtration rate (GFR). If the patient has compromised renal function, one could consider using generous intravenous hydration with normal saline prior to and after the procedures. Patients should be asked regarding their medication history, especially with regard to any blood-thinning medications, and allergies, including those to intravenous contrast media. Patients with an allergy to intravenous contrast can be pre-medicated prior to TAE according to institutional protocols which typically include a combination of diphenhydramine and oral steroids. Blood thinning medications should be held according to published guidelines [25]. The pre-procedural consultation also provides the IR with the opportunity to determine whether the patient will be able to proceed with the procedures using moderate conscious sedation or will require general anesthesia. The majority of patients should be able to comfortably tolerate both procedures with moderate conscious sedation but an individualized approach for each patient is recommended. After a discussion of these items with the patient, informed consent is obtained.

**Procedural Technique for TAE of the Renal Mass**

The patient is supine on the angiography table. Prophylactic antibiotics are not routinely used [26]. The arterial access site (typically the right common femoral artery) is prepared and draped in standard sterile fashion. At our institution, we gain vascular access under sonographic guidance using a micro-introducer kit after the instillation of lidocaine for local anesthesia. After access is obtained and a vascular sheath is placed, a flush catheter (OmniTM Flush, AngioDynamics, Latham, NY, USA) is then inserted over the wire and an aortogram is obtained (fig. 1A). The purpose of the aortogram is to identify the location of the renal arteries and assess for any vascular anomalies, such as supernumerary renal arteries. The flush catheter is then exchanged over a wire for a diagnostic catheter that is used to select the appropriate renal artery. The authors prefer a reverse curve catheter, such as the 5F SOS 2 OmniTM (AngioDynamics, Latham, NY, USA) or 5F Sim 1 (Terumo, Somerset, NJ, USA), although many other diagnostic catheters would also suffice. Once the appropriate renal artery is selected with the diagnostic catheter, angiography is again performed in order to identify the tumor, assess its vascularity, and plot the appropriate course for sub-selection of the renal arterial system (fig. 1B). The renal artery or arteries supplying the tumor are then selected using a micro-catheter and micro-wire. There are many combinations of micro-catheters and micro-wires that would be appropriate for use in this situation; although, the authors would advise using a straight-tipped, high-flow (2.7F or 2.8F) microcatheter in order to easily accommodate the embolic material. Once the renal artery or arteries supplying the tumor are selected, angiography is again performed to confirm catheter location prior to embolization (fig. 1C).

The choice of embolic material is operator dependent as there is insufficient evidence to say that any one particular embolic approach is superior in RCC [17–24]. Specific types of embolics are discussed to provide the
practitioner with the benefits and drawbacks of each. Particles, such as Embospheres® (Merit Medical, South Jordan, UT, USA), are permanent embolic agents that are easy to use and familiar to most IR physicians. Varying sizes of particles can be used depending on the size of the supplying arteries but even the smallest particles may not penetrate to the capillary level. Ethanol, a liquid embolic, has a long history of use in treating RCC [27]. Since it is a liquid, ethanol has the ability to penetrate to the smallest vessels of the tumor, thereby making it an extremely effective agent for inducing ischemia and tissue death. When embolizing with ethanol, one must be cognizant of the patient’s hemodynamic status as pulmonary hypertension can occur when ethanol is used [28]. Coils and micro-coils are common embolic agents that are familiar to most IR physicians. They are easy to deploy and rapidly induce thrombosis in the target vessel. Yet, a drawback of coils is that they fail to penetrate deeply into the target tissue when compared to particles or ethanol.

Regardless of the agent, embolization is performed until stasis is achieved in the target vessels (fig. 1D).

All embolization is performed under careful fluoroscopic guidance to prevent reflux of embolic agent into non-target vessels. To achieve this, embolic agents like particles or ethanol need to be mixed during the procedure with either contrast or ethiodized oil. Ethiodized oil in and of itself can be used as an embolic agent; however, it is most commonly used to make other embolic agents visible during fluoroscopy. One advantage to using ethiodized oil (as opposed to contrast) is its retention within tumor tissue that can serve to localize RCC during computed tomography (CT)-guided percutaneous ablation. Often, localizing the mass prior to ablation probe placement is not difficult on the non-contrast CT images obtained during the ablation. Nonetheless, there are occasions when localizing the RCC can prove to be difficult, such as when there are multiple masses or cysts in the same kidney, small tumors, and endophytic tumors.
If ethiodized oil is used during the TAE, visualization and localization of the RCC are enhanced (fig. 2). The improved localization and visualization from ethiodized oil can provide the operator with the confidence that the entire lesion is being treated during the ablation session. This feature becomes particularly important when one considers that incomplete ablation of the tumor margins may have stimulatory effects on tumor progression secondary to alterations in the tumor micro-environment [29]. Therefore, ethiodized oil has a dual function which includes allowing visualization of the embolic material during TAE and localization of the RCC during CT-guided percutaneous ablation.

**Fig. 2.** A Axial slice from a contrast-enhanced CT in portal-venous phase in the same patient as figure 1 obtained prior to both TAE and percutaneous ablation shows an enhancing 3.9 cm RCC in the upper pole of the right kidney (white arrow). The anterior and posterior of the patient are labeled in each figure for orientation. B Pre-ablation CT obtained in prone position for the same patient as figure 1. Since the 3.9 cm right RCC was embolized using particles mixed with ethiodized oil, the mass is easy to identify because of the retained oil (white arrow). The white dots seen along the skin (white arrowheads) represents the paper localizing grid. C Axial slice from a contrast-enhanced CT in portal-venous phase in a 55-year-old man with a 2.8 cm enhancing RCC in the upper pole of the left kidney (white arrow). D Pre-ablation CT in the same patient as figure 3C in right lateral decubitus position. This mass (white arrow) was embolized with particles alone and is much more difficult to differentiate from normal renal parenchyma than the mass in figure 3B. This highlights the advantages of using ethiodized oil as a contrast agent. The paper localizing grid (white arrowheads) is seen.

**Fig. 3.** A 53-year-old male with a 2.3 cm RCC in the left kidney. A, Pre-ablation CT with the patient in prone position demonstrates the exophytic mass in the left kidney (white arrow). The paper localizing grid is seen (white arrowheads). The anterior and posterior of the patient are labeled in each figure for orientation. B After localizing the tumor, a cryoablation probe is advanced into position under CT guidance (white arrow). C CT scan obtained after 5 minutes of cryoablation shows the tip of the ablation probe with the surrounding hypodense “ice ball” (white arrow). The iceball allows the IR to monitor the progress of the procedure and adjust treatment as necessary. The RCC (white circle) is within the ablation zone. A 22G needle (double white arrow) was inserted under CT guidance prior to ablation in order to instill normal saline (white arrowhead) in between the tumor and the colon (white asterisk). This technique is known as “hydrodissection” and can be used to protect normal structures from the ablation zone. D CT scan obtained after 10 minutes of cryoablation shows the tip of the ablation probe with an enlarging iceball (white arrow). The RCC is again well-within the ablation zone (white circle). The 22 G needle and hydrodissection fluid are again noted. An appropriate distance from critical structures is maintained.

**Procedural Technique for Percutaneous Ablation of the Renal Mass**

There is no well-defined time point at which ablation should follow TAE [17–24]. It is our preference to perform percutaneous ablation under CT guidance; although, ultrasound could also be used in select patients. Peri-procedural antibiotics may be given according to accepted guidelines [26]. An intra-procedural CT scan is obtained in order to localize the lesion but patient positioning on the CT table is dictated by the best percutaneous access to the RCC. As discussed, identifying the RCC to be treated may not prove difficult, especially if ethiodized oil is used during TAE. However, operators
may rely on anatomic landmarks or give intravenous contrast in order to identify the RCC. The percutaneous access site is then prepared and draped in standard sterile fashion. The site or sites are anesthetized with lidocaine. The choice of ablation probe is operator-dependent as there is insufficient evidence to say that any ablative modality is superior to the others in RCC [30]. The authors prefer to use cryoablation probes (BTG, West Conshohocken, PA, USA) for RCC. Cryoablation allows the operator to more closely supervise the ablation zone by the formation of an “ice ball” that is readily apparent under CT (fig. 3). Cryoablation, however, does take longer than microwave ablation. Other ablative techniques, such as radiofrequency ablation and irreversible electroporation, may also be considered in the appropriate patients. Once the lesion is clearly identified, ablation probes are advanced into the RCC under CT guidance.

Once the probes are in place, many operators will perform a percutaneous biopsy of the lesion prior to treatment [30]. At this point, the operator should review the images to assure that any critical structures such as bowel, aorta, inferior vena cava, renal pelvis, and ureter are well outside the ablation zone prior to proceeding. If there is a question of encroaching upon these areas with the ablation zone, then adjunctive techniques such as hydrodissection or pneumodissection can be performed via a 22 G needle (fig. 3C, 3D). Finally, ablation is performed according to the probe’s instructions for use with intermittent imaging to assess the progress of the ablation (fig. 3). Once the ablation is complete, a final CT scan is obtained that covers from the lung bases to the pelvis in order to assess for tumor coverage and any potential complications. If the patient is to be discharged home, the authors watch the patient for 4–6 hours after the procedure; otherwise, they are admitted for overnight observation. For follow-up, we see the patient back in approximately 2 weeks to assure adequate pain control and the absence of any complications (i.e. persistent hematuria, urinary retention). We then obtain either a contrast-enhanced CT or MRI with a renal mass protocol at 3, 6, and 12 months post-procedure. Then, if there is no sign of recurrent or residual tumor, we will follow the patient with imaging at yearly intervals for 3–5 years.

Institutional Experience

Institutional review board approval was obtained to access medical records for retrospective review of patients who have undergone TAE prior to percutaneous renal mass ablation therapy. Descriptive and comparative statistics were calculated with JMP v.10 (Cary, NC, USA). All continuous variables are presented as means and compared with $t$-tests.

After a review of our radiology information system, we identified 11 patients (6 males and 5 females) with a mean age of 67.7 years (range 52–85 years) who had undergone TAE prior to percutaneous ablation. All patients had a single RCC with mean tumor diameter of 50.2 mm (range 28–84 mm). Patients were referred to IR for percutaneous ablation (rather than surgery) for the following reasons: presence of a second malignancy, chronic kidney disease, advanced age, severe chronic obstructive pulmonary disorder, congestive heart failure, morbid obesity, prior surgical history that would increase operative risk, and patient preference. Patient selection for TAE prior to percutaneous ablation was made by the treating IR in conjunction with the referring urologist. Per review of the notes, the decision to proceed with the combined approach was influenced by a larger tumor size or the suggestion of a highly vascular lesion on pre-procedural imaging.

One patient underwent TAE of their RCC under general anesthesia due to patient preference while the remainder was performed with moderate conscious sedation. All TAE of RCC were performed as out-patient procedures except for 1 patient who was already hospitalized due to symptomatic hematuria. RCCs were embolized with particles alone ($n = 4$), particles mixed with ethiodized oil ($n = 2$), ethanol and ethiodized oil mixture ($n = 2$), ethanol followed by particles ($n = 1$), particles followed by micro-coils ($n = 1$), and micro-coils alone ($n = 1$). TAE embolization of the RCC was technically successful in each case and we had no complications.

We performed percutaneous ablation at a mean of 9.1 days (range 1–20 days) after TAE. For this procedure, general anesthesia was used in 2 patients due to either patient or IR physician preference. It is our typical practice to perform percutaneous ablations as out-patient procedures; however, in this cohort, only 2 patients had percutaneous ablation as an out-patient while the majority were observed overnight after ablation. Per review of the notes, the decision was made to monitor patients clinically overnight because of the size of the lesions that were ablated. Percutaneous ablation was done with cryoablation in 10 patients and with microwave ablation in 1 patient due to IR physician preference. Ablation was technically successful in all but 1 patient (a cryoablation patient where the ablation was purposefully stopped short of the margin secondary to its proximity to
the renal hilum). We’ve had 3 Clavien Grade I complications (all perinephric hematomas), which all occurred after cryoablation, but none required treatment. Four patients required repeat cryoablation for residual tumor (all of these patients had a tumor diameter of > 5 cm). One additional patient required repeat cryoablation due to recurrent disease 13 months after the initial treatment. The remaining 6 patients have all had adequate tumor control. Follow-up on these patients ranges from 13 to 91 months. Importantly, we also found that patient GFR did not change significantly subsequent to TAE combined with percutaneous ablation (p = 0.84). This is significant given that a legitimate concern regarding this approach is that the embolization and added contrast load to the kidney may adversely affect renal function, thereby outweighing the potential benefits. However, we have not found this to be the case.

**Brief Literature Review**

TAE as an adjunctive therapy for RCC prior to percutaneous ablation has the potential benefits of improving local tumor control, protecting against renal hemorrhage, and enhancing tumor localization during ablation [24]. This technique has been described in the radiology literature dating back to 2000 with a case report of a single RCC being embolized with 300 µm particles prior to radiofrequency ablation in order to reduce procedural bleeding [23]. Since that time, there are scattered case reports and cohort studies in the literature showing the technique to be both safe and feasible [17–23]. For example, Yamakado et al. [17] theorized that this technique would be of most benefit in RCC larger than 3.5 cm. They treated 12 RCCs in 11 patients (all > 3.5 cm in size) with combined TAE and percutaneous radiofrequency ablation and demonstrated tumor control in all lesions at 13 months with a delayed abscess in 1 patient. The largest published cohort to date examined the results of TAE prior to radiofrequency ablation in 36 RCCs (mean diameter 3.1 cm; range 1.2–6.5 cm) in 31 patients [20]. The authors of this study embolized the RCCs with ethanol mixed with either ethiodized oil or polyvinyl alcohol 6 days prior to percutaneous radiofrequency ablation. In this group, there were no recurrent tumors for patients with RCC < 4 cm even though the recurrence rate was 2.8% overall. No major complications were reported. More recently, Nakasone et al. [18] retrospectively analyzed the effects of TAE with ethiodized oil and gelatin sponges followed immediately by percutaneous radiofrequency ablation in 10 patients with 12 RCCs (mean diameter 3.1 cm; range 1.8–6.6 cm). The authors were technically successful in all patients for both procedures. No major complications were reported. At a follow-up of approximately 4 years, there were no recurrences and, importantly, no significant effect on patient GFR. In summary, TAE of RCC prior to percutaneous ablation is technically feasible and does not adversely affect patient outcomes. It is a technique that may be considered in patients with large or hyper-vascular RCCs. Certainly, more study is warranted to demonstrate its clinical benefit. Further investigations should include prospective data and the evaluation of newer ablative technologies such as cryoablation, microwave ablation, and irreversible electroporation.
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