Role of Embolization in the Treatment of Renal Masses

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Abstract

Renal arterial embolization (RAE) performed for the treatment of renal masses has been proven to be a safe and effective technique, with several decades of experience. RAE is well tolerated with few complications, particularly if the time interval from embolization to surgery is reduced to less than 48 hours. Review of the literature suggests that RAE is also extremely effective for palliation of symptoms in the setting of nonoperative advanced stage renal cell carcinoma. In addition, this technique plays a large role in the management of angiomyolipomas that are symptomatic or at risk of spontaneous rupture. To date, RAE has not been evaluated in a randomized controlled setting, which has contributed to its underutilization. All of these potential benefits warrant the need for prospective studies for further validation.

Keywords
- embolization
- renal cell carcinoma
- angiomyolipoma
- preoperative
- interventional radiology

Objectives: Upon completion of this article, the reader will be able to describe the role of embolization of renal cell carcinoma and angiomyolipoma, both as adjunctive as well as definitive therapy.

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Renal cell carcinoma (RCC) is the most common malignant renal tumor, comprising an estimated 2 to 3% of all malignancies with an estimated 64,770 new cases diagnosed in the United States[1] in 2012. Common symptoms associated with RCC include hematuria, flank pain, and a palpable mass. Patients presenting with symptoms usually have advanced stage disease. The natural history of RCC has changed, with the majority (~70%) now diagnosed incidentally on routine abdominal imaging.[2] Despite the associated stage migration due to increase in incidental detection, there remain a significant proportion of patients presenting with advanced stage disease. Approximately 30 to 40% of patients with renal tumors will either present with or later develop metastatic disease, and death rate from RCC remains high, with 13,570 disease-related deaths[1,2] in 2012.

Prognosis significantly changes with stage, ranging from a 5-year overall survival (OS) of 90% for localized disease to 10% for advanced stage disease.[1] For localized RCC, surgical resection is the treatment of choice. Partial nephrectomy (nephron-sparing surgery) to preserve renal function is preferred over radical nephrectomy if technically feasible and has been shown to not compromise survival outcomes.[1,2] For patients unable to undergo surgery, local ablative therapies remain an option.

Renal angiomyolipoma (AML) is the most common mesenchymal renal tumor, with a reported incidence of 0.3 to 3% in the general population.[3,4] Renal AMLs can occur either in a sporadic form or in association with tuberous sclerosis (TS). AMLs are generally considered to be benign; though in rare

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cases, it can be locally aggressive with either extension into the renal vein and inferior vena cava or dissemination into adjacent lymph nodes.[4] AMLs are typically asymptomatic and found incidentally on imaging. However, a minority present with hematuria, flank pain, or spontaneous hemorrhage. Thus, treatment of symptomatic AMLs or those at risk of hemorrhage is recommended.[5–7]

Almgård first popularized renal artery embolization (RAE) in the 1970s and initial interest in the technique resulted in multiple published series in the 1980s and 1990s.[8–10] Indications for RAE for the treatment of renal masses include as an adjunctive preoperative treatment before nephrectomy for primary kidney masses; palliation of symptoms related to advanced stage RCC; and primary treatment of AML.

Anatomic and Technical Considerations

Multiple previous review articles have detailed the anatomic and technical considerations for RAE.[9–11] Classically, single renal arteries arise from the abdominal aorta at the level of the L1–L2 interspace. The main renal arteries branch into anterior and posterior divisions, followed by segmental, lobar, interlobar, and arcuate arteries. Variant anatomy can occur in greater than 30% of the general population, with either early division of the main renal arteries or extrarenal arteries further subdivided into accessory (hilar) or aberrant (polar) entry into the kidney.

Arterial vascular access is typically gained via the right common femoral artery and a vascular sheath (5 French) placed. Through the vascular sheath, aortography can be performed to locate the origin of the renal arteries with a flush catheter placed slightly superior to the expected origin of the renal arteries. Selection of the renal arteries is performed with shaped catheters such as a SOS-shaped, Cobra, or Simmons-shaped catheter. Superselective catheterization of the renal arteries can be performed with a microcatheter and microwire. Embolization materials can be introduced into the desired target vessels. If ethanol is chosen as the embolic material, occlusion balloon catheter delivery systems are typically used.

There is wide variation in embolization agents used for RAE as highlighted in ►**Table 1**. No specific agent has been demonstrated to be more efficacious than others in the setting of RAE. Several principles specific to RAE should be noted in choosing an embolic agent. First, vessels in the kidney are considered "end arteries" without significant intrarenal collaterals. Second, RCCs are hypervascular tumors that recruit extrarenal collateral vascular supply. As such, utilization of an agent that results in permanent small vessel/capillary bed occlusion/sclerosis such as NBCA glue, ethanol, PVA, or Embospheres (Merit Medical, South Jordan, UT) in addition to large vessel occlusion with coils is desired.[11–15]

Results

Current indications for RAE include palliation for advanced stage RCC; preoperative embolization before nephrectomy; treatment for angiomyolipoma; and as an adjunctive therapy to ablation for RCC.

To date, no prospective randomized controlled clinical trials have been performed to evaluate the role of RAE in these settings. In 1999, Kalman and Varenhorst published a survey of the pertinent literature on RAE, which was later adapted by Madoff et al in 2006.[9,10]

►**Table 1** highlights some of the limitations of the previous evidence accumulated in the 20th century. These studies were limited by design, many being observational with significant variation in both patient selection criteria and embolic agents used, making it difficult to draw firm conclusions.

Given the wide variation in results and lack of strong clinical evidence, preoperative RAE has largely fallen out of favor. Scattered case series have been published since 2000 as summarized in ►**Table 2**, and have not altered the role of RAE.

Preoperative Embolization

Benefits of RAE in the preoperative setting include a decrease in perioperative blood loss, creation of a tissue plane of edema facilitating dissection, and reduction in tumor bulk including extent of vascular thrombus, when present. Wide variation in reporting markers such as reduction in intraoperative blood loss, transfusion requirements, surgical procedure time, surgical complications, and survival outcomes has limited its use to local practice patterns[10] (►**Fig. 1**).

In an observational study by Schwartz et al performed at the authors' institution, there was a perceived benefit of both decreased intraoperative transfusions and operative time.[15] The study population included those with advanced stage disease with mean tumor size of 11.2 cm. Almost half of all patients had vascular invasion, with reported blood loss of only 1,048 mL (median 725 mL) and average patient transfusion requirements over their entire hospital course of 3.9 units. In the subset of patients who did not have vascular invasion, mean blood loss was lower (mean 647 mL, median 425 mL). Described complications were minor (none requiring hospitalization) and surgical times and survival outcomes were not analyzed.

Recent studies by May et al and Zielinski et al include case-controlled matched historical cohorts with survival outcomes that are contradictory.[16,17] May et al concluded no survival benefit from RAE, while Zielinski et al concluded significant survival benefit. This difference may be a result of different selection processes of the control groups. In the study by Zielinski et al, controls were chosen from the same historical cohort and matched in age, sex, tumor size, grade, and stage. In the report by May et al, controls were chosen from the timeframe of 1992 to 2006, with baseline oncology characteristics matched based on propensity scores to the RAE cohort performed within the timeframe of 1992 to 1997. In both series, surgical complications were similar in both control and RAE groups; intraoperative blood loss and intraoperative times were not directly evaluated. May et al did demonstrate increased postoperative transfusion requirements in the RAE cohort.

Subramanian et al provided comparisons of those undergoing preoperative RAE to controls in regard to intraoperative times, blood loss, and immediate perioperative complication and mortality rates.[18] In this study, preoperative RAE was

Table 1 Case series published in the English literature, in order of year of publication, agents used for therapeutic embolization, number of patients, and indication for embolization

First author	Year of publication	Method	Number of patients	Preoperative	Palliative	Not specified
Almgård[8]	1977	Muscle particles	38	29	9	
Frasson[53]	1978	Gelfoam	45	35	10	
Schulman[54]	1980	Coils Gelfoam Gelfoam + coils ICBA	3 10 9 4	26	2	
Frasson[55]	1981	Coils Gelfoam Gelfoam + coils ICBA Muscle particles	6 226 3 7 2	241	41	
Giuliani[56]	1981	Coils Gelatin foam ICBA	1 14 25	40		
Kato[57]	1981	Encaps MMC + gel sponge	33	23	10	
Mobilio[58]	1981	Gelfoam ICBA	41 1	41 1		
Wallace[38]	1981	Gelfoam + coils	100	74	26	
LeGuillou[59]	1982	Not specified	247	203	44	
Teasdale[60]	1982	Coils Gelfoam Gelfoam + coils	3 22 3	26	2	
Bono[61]	1983	Avitene Gelfoam ICBA	47 48 4	47	48	4
Nakano[62]	1983	Gelatin sponge ICBA	21	12	9	
Ekelund[63]	1984	Ethanol	20	6	14	
Kaisary[64]	1984	Coils Gelatin sponge Lyodura Thrombin Combinations of above	25	25		
Kurth[65]	1984	Coils Ethanol Gelfoam ICBA Thrombin	25	25		
McIvor[66]	1984	Coils Dura particles Gelfoam Thrombin	29	29		
Mebust[67]	1984	Coils + gelatin sponge Ethanol	41 5	40	6	
Christensen[68]	1985	Coils	36	36		
Gottesman[69]	1985	Coil + Gelfoam	30	30		
Klimberg[70]	1985	Ethanol	25	24	1	
Lammer[71]	1985	Coils Ethanol Gelfoam Ivalon	4 7 85 25	81	40	

Table 1 (*Continued*)

First author	Year of publication	Method	Number of patients	Preoperative	Palliative	Not specified
Leinonen[72]	1985	Ethanol Gelfoam	12 18	10 11	2 7	
Weigel[73]	1985	Coils Ethanol Gelfoam	22	22		
Chudácek[74]	1986	Ethibloc Gelaspon Vilan	30		30	
Karwowski[75]	1987	Gelfoam Gelfoam + coils	81 39	30	39	
Kurth[76]	1987	Coils Ethanol Gelfoam ICBA	33	33		
Nurmi[77]	1987	Ethanol Ethanol + coils Gelfoam Gelfoam + coils ICBA ICBA + coils ICBA + coils + Gelfoam	4 3 3 2 10 2 1		25	
Stoesslein[78]	1988	Detachable balloons Histoacryl Ivalon Combinations	147	100	47	
Swanson[79]	1988	Coils Gelfoam Ivalon Gelfoam + BCG	134 11	145		
Kato[80]	1989	Encaps MMC Encaps MMC + Gelfoam	44 129	99	74	
Lanigan[81]	1992	Ethanol	35	35		
Bakal[82]	1993	Ethanol Ethanol + coils Ethanol + Gelfoam	22 1 1	22 1 1		
Park[83]	1994	Ethanol	27	27		

Abbreviations: BCG, Bacillus Calmette-Guerin; ICBA, isobutyl-2-cyanoacrylate; MMC, microencapsulated mitomycin.
Source: Printed with permission from Madoff et al,[10] originally adapted from Kalman and Varenhorst[9]).

associated with increased median operative times (390 vs. 313 minutes), median intraoperative transfusion requirements of 8 versus 4 units of packed red blood cells, and perioperative mortality of 13% versus 3%. However, the control population was not equal with the preoperative RAE group, with the latter being composed of patients of higher tumor stage, American Society of Anesthesiology (ASA) scores, and need for the use of intraoperative cardiopulmonary bypass.

Palliation

Several recent small series ($n = 8$–25 patients) have focused on RAE in the setting of palliation,[19–22] demonstrating favorable results for symptom control. Treatment indications commonly included palliation of hematuria and/or flank pain, and less commonly control of paraneoplastic syndromes and palpable masses. Mukund and Gamanagatti demonstrated symptom control in 7/8 (88%) patients, with gross hematuria controlled in 6/7 (86%) patients and flank pain controlled in 1 patient at 6 months.[20] Maxwell et al demonstrated symptom control in 18/19 (95%) patients with hematuria controlled in 13/13 (100%) patients and flank pain in 8/9 (89%) patients.[19] Munro et al also demonstrated a 70% effectiveness in symptom control, with only a 12% rate of recurrent hematuria requiring hospital admission.[21] Onishi et al[22] compared 30 historical controls with 24 patients who underwent RAE who were matched for age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, and stage. Similar to the other studies, RAE was 75% effective in symptomatic control (14 patients with gross hematuria and 5 patients with flank pain).

Table 2 Case series published in the English literature since 2000 for renal arterial embolization performed in the setting of renal cell carcinoma, in order of year of publication, number of patients, indication for embolization, conclusions, and study limitations

First author	Year of publication	Number of patients	Indication	Study conclusions	Study limitations
Zielinski[17]	2000	118	Preoperative	RAE with improved overall 5- and 10-y survival as compared with 116 case-matched controls (62 vs. 47, 35 vs. 23%) particularly for T2, T3, and node-positive disease	Single center Variability in time delay from embolization to surgery (Only 56% performed 1–3 d before surgery) Variability in embolization agents
Onishi[22]	2001	24	Palliation	RAE effective in palliation with 75% improvement in symptoms and increased overall survival (229 vs. 116 d) compared with similar controls	7-mo overall survival of RAE poorer than 17.8 mo reported for cytoreductive nephrectomy, though cohort of this study had poorer performance status
Munro[21]	2003	25	Palliation	RAE effective in palliation with 70% improvement in symptoms	
Maxwell[19]	2007	19	Palliation	RAE effective for palliation with 18/19 symptom control	
Schwartz[15]	2007	121	66 preoperative 15 AML 13 vascular lesions 8 palliation 19 other	RAE well tolerated with minimal complications, and suggestion of improved intraoperative times and decreased blood loss in the perioperative setting	Outcomes study with no matched controls for comparison
May[16]	2009	227	Preoperative	RAE with no difference in overall survival and trend toward worsened cancer-specific survival as compared with oncologic matched controls	Poor control matching with controls taken from 1992 to 2006 as compared with a RAE historical group (1992–1997) Coils used as the sole embolic agent in 95% of cases
Subramanian[18]	2009	135	Preoperative advanced stage RCC with IVC involvement	RAE with no measurable benefit in reducing blood loss or perioperative complications, with increased perioperative mortality and trend toward increased transfusion requirement	Poor control matching with embolization group with increased ASA scores in 3–4 (97 vs. 90%), increased vascular tumor thrombus extent (66 vs. 48%) level III–IV, and use of vascular bypass (52 vs. 28%)
Mukund[20]	2010	8	Palliation	88% effective at palliation of symptoms	Small series of case reports

Abbreviations: AML, angiomyolipoma; IVC, inferior vena cava; RAE, renal artery embolization; RCC, renal cell carcinoma.

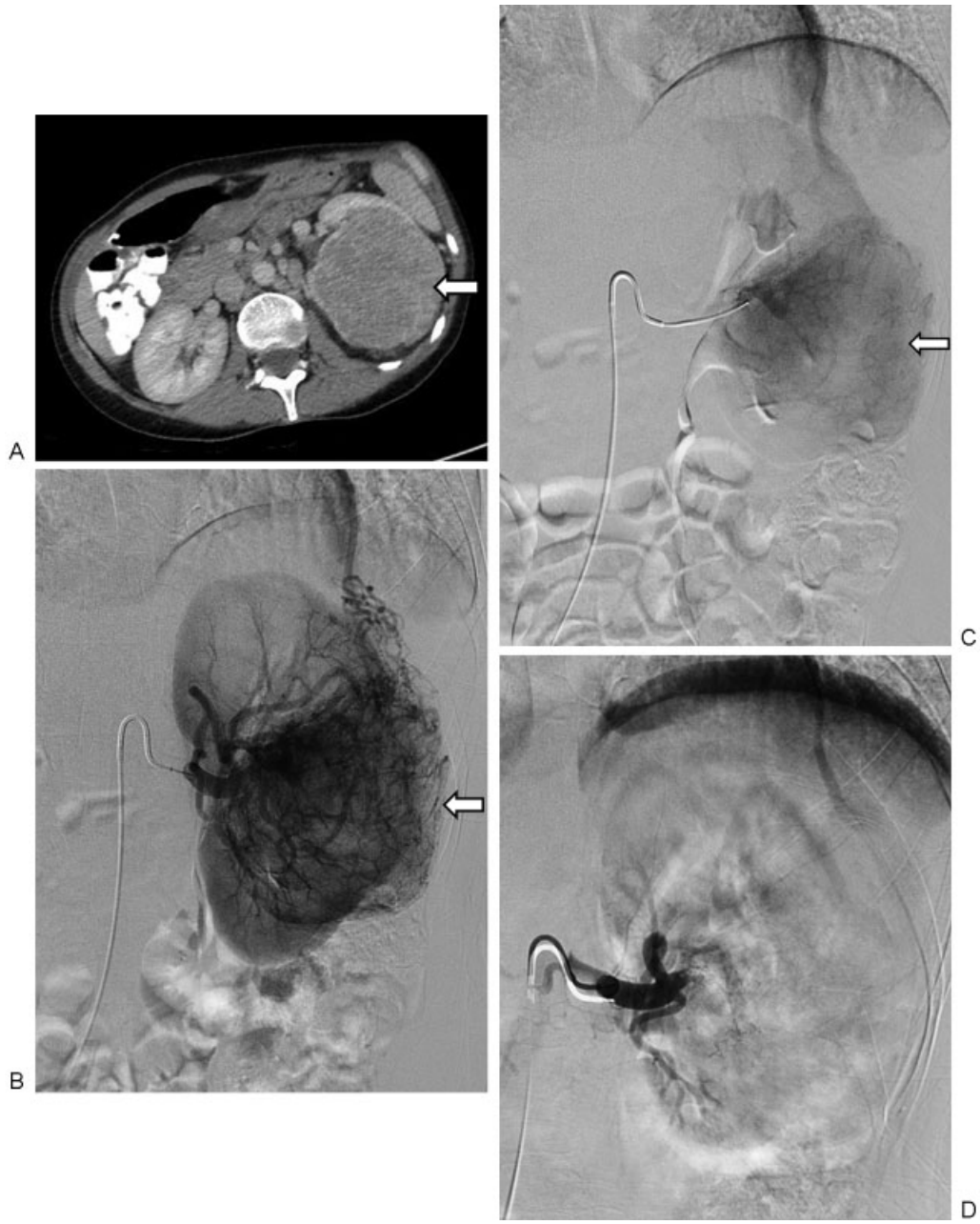

Figure 1 A 53-year-old woman with 11.7 cm left renal cell carcinoma that underwent preoperative left renal arterial embolization followed by uneventful left nephrectomy with a reported total estimated blood loss of 300 mL. (A) Axial contrast-enhanced computed tomography image of the enhancing left renal mass (arrow). (B) Selective left renal arteriogram demonstrating a large hypervascular renal cell carcinoma (arrow) before embolization. (C) Microcatheter-mediated embolization of the hypervascular mass using tris-acryl gelatin microspheres to stasis. Note the decreased regions of tumor vascularity (arrow). (D) Postembolization selective left renal arteriogram demonstrating near-complete embolization of the left renal artery to stasis.

Interestingly, the RAE group showed a statistically significant median survival benefit of 229 versus 116 days for the control group, suggestive of a possible improvement in outcome either through a cyto-reductive effect or via immunomodulation. This result, while encouraging, is still inferior to surgical palliation, with 7-month median survival in the RAE group versus 17.8 months median survival gained in the setting of palliative nephrectomy.[23]

RAE in the setting of palliation is well tolerated, although postembolization syndrome is common after RAE (reported in 14/24 (57%) patients in one study). Postembolization syndrome is well controlled with antipyretics, analgesics, and antiemetics, usually resolving in 3 days. Median hospital stay after RAE is 4 to 5 days.

Treatment for Angiomyolipoma

RAE is well established as the first-line therapy for the treatment of AML. Indications for RAE include symptomatic AMLs such as those with prior or active hemorrhage, flank pain, hematuria, or mass effect. AMLs larger than 4 cm have

been shown to be associated with symptoms (80–90%) and spontaneous hemorrhage (50–60%). Therefore, prophylactic treatment of AMLs greater than 4 cm serves as another indication for RAE[24–26] (►**Fig. 2**). Multiple retrospective series have been published since 2000 that provide long-term follow-up confirming safety and long-term efficacy of RAE for AML (►**Table 3**).

These studies show overall durable tumor treatments with low surgical salvage rates, with recurrence rates ranging from 0 to 37%. The majority of recurrences are successfully managed with repeat RAE. Complications are rare with no episodes of renal insufficiency attributable to embolization documented in any series.[27] Postembolization syndrome is the most common complication, occurring in up to 64% of patients in one series. Most cases are self-limited and successfully treated with antipyretics and nonsteroidal anti-inflammatories. Major reported complications are limited to abscess formation, coagulative necrosis, and self-limited nontarget embolization to normal renal parenchyma, all successfully treated without long-term adverse sequelae.

The proven efficacy of nephron sparing surgery (NSS) in the setting of RCC has renewed interest in surgical options for AML, and multiple recent series evaluating the use of NSS as an alternative to embolization for AMLs have been published.[28–31] Proponents of NSS as compared with embolization for AML argue that NSS provides more durable outcomes and also offers pathology in case of malignancy. However, NSS has increased long-term adverse sequelae associated with the procedure, with Boorjian et al reporting a 5% urinary leak rate and Heidenreich et al reporting a 7% urinary fistula rate.[28,30] Therefore, NSS is currently limited to the setting of failed RAE.

The choice of embolization agent for AML is controversial. Common agents include ethanol, PVA, and Embospheres (Merit Medical). The use of Onyx (Covidien, Plymouth, MN) in AML treatment has also been reported.[32] The utility of coils remains unclear with some authors advocating their use, and others suggesting that their use promotes collateral formation around the level of occlusion. Lenton et al reported a high intraprocedural aneurysm rupture rate (30%) as compared with most groups that reported no episodes of rupture. These authors conveyed that this may be attributed to the use of PVA alone rather than PVA and coils.[33] Villalta et al found that smaller microspheres (< 150 µm) were associated with both an increased recurrence rate requiring repeat embolization

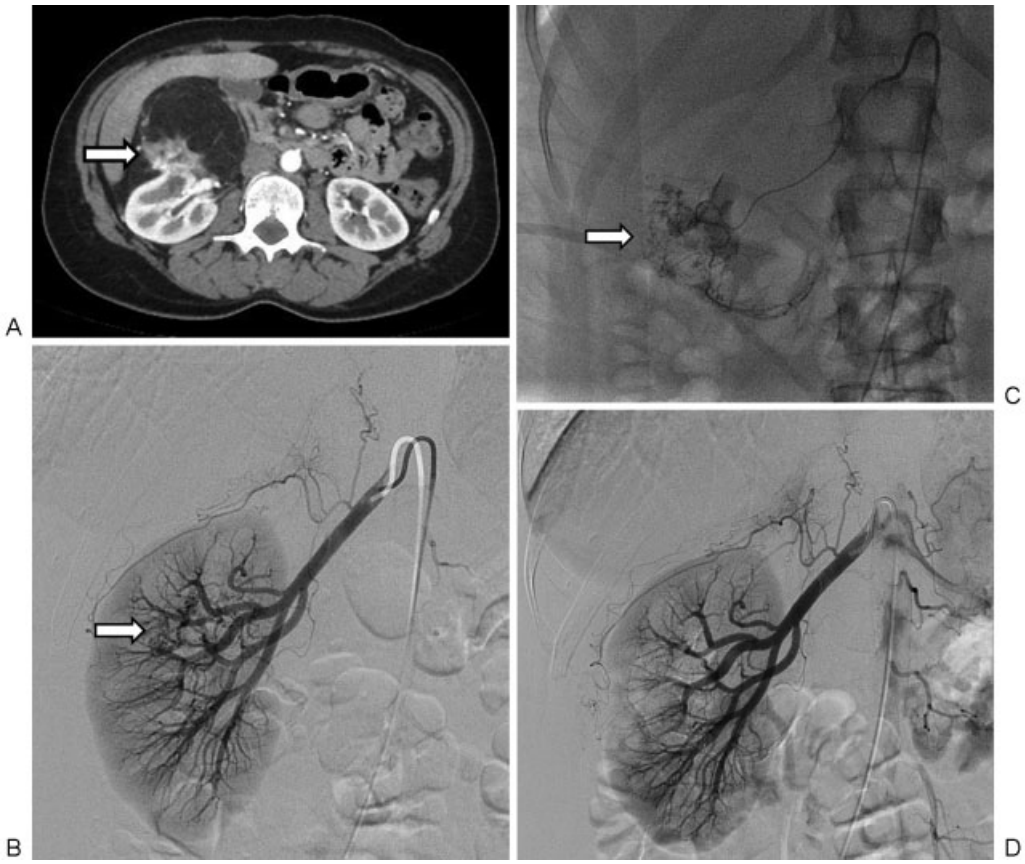

Figure 2 A 45-year-old woman with incidental 9.4 cm right renal angiomyolipoma that underwent renal arterial embolization. (A) Axial contrast-enhanced computed tomography image of angiomyolipoma demonstrating predominantly fatty components, vascular components (arrow), and origin of the mass from the kidney. (B) Selective right renal arteriogram demonstrating a small area of heterogeneity and hypervascularity overlying the midpole region of the right kidney (arrow). (C) Microcatheter-mediated embolization of the hypervascular aspects of the mass using tris-acryl gelatin microspheres to stasis (arrow). (D) Postembolization selective right renal arteriogram demonstrating complete embolization of the right AML.

Table 3 Case series published in the English literature since 2000 for renal arterial embolization performed in the setting of angiomyolipoma, in order of year of publication, number of patients, mean size, indication for embolization, embolization agents and outcomes

First author	Year of publication	Number of patients	Mean size (cm)	Indication	Agents	Outcomes
Ewalt[36]	2005	16 with 27 AMLs (16 TS)	Not specified:4–21 range	13 symptomatic 3 asymptomatic	PVA or Embospheres (50–750 μM) + fibered coils	No documented recurrence with 7 patients followed up 3–9 y
Kothary[5]	2005	19 with 30 AMLs (9 sporadic/10 TS)	Not specified	16 symptomatic 3 asymptomatic	Ethanol + lipiodol (1 also with coils)	31.6% recurrence rate all in TS group with mean f/u 51.5 mo Median time to recurrence 78.7 mo (mean 81.3)
Williams[37]	2006	16 with 20 AMLs (16 TS)	Not specified		PVA (200–1,200 μM) + liquid coils (3 also with stainless steel coils)	No documented recurrence or rehemorrhage with mean f/u of 40 mo
Lenton[33]	2008	17 (5 sporadic/12 TS)	Not specified	13 symptomatic 4 asymptomatic	PVA (350–500 μM) +/− coils	29% recurrent treatment rate with repeat embolization
Chick[84]	2010	34 (16 with multifocal AML) (25 sporadic/9 TS)	11.9 (2.9–24.4)	26 symptomatic 8 asymptomatic	Ethanol + lipiodol (2 also with PVA and 3 also with coils)	15% recurrence rate with mean f/u of 44.2 mo. 2 patients with repeat embolization and 3 with surgery offered
Lee[85]	2009	11 (7 sporadic/4 TS)	8.6 (4.5–12.8)	9 symptomatic 2 asymptomatic	Gelfoam + coils	18% recurrence rate with mean f/u of 28.2 mo. 1 recurrence with nephrectomy at 40 mo another with repeat embolization at 2 mo and 7 y
Ramon[6]	2009	41 with 48 AMLs (33 sporadic/8 TS)	10.3 (2.5–20)	21 symptomatic 21 asymptomatic	Ethanol + PVA (50–150 μM) and coils in 7 cases	29% predicted recurrence rate at 5 y from Kaplan–Meyer estimates (71% reembolization free survival) and 3 with surgery offered (94% surgery free)
Takebayashi[86]	2009	10 with 10 AMLs (10 Sporadic)	7.0 (4.5–11.0)	10 asymptomatic	Ethanol	No documented recurrences at mean f/u of 2.2 y

(*Continued*)

Table 3 (*Continued*)

First author	Year of publication	Number of patients	Mean size (cm)	Indication	Agents	Outcomes
Bishay[87]	2010	16 with 23 AMLs (4 sporadic/12 TS)	15 (10–25)		Ethanol + lipiodol	19% recurrence rate requiring repeat embolization with mean f/u of 29 mo (1 failure with hemorrhage at 59 mo requiring repeat embolization)
Chan[35]	2011	27 with 28 AMLs (26 sporadic/1 TS)	10.9 (4–30)	15 symptomatic 13 asymptomatic	Microcoils Ethanol + lipiodol Ethanol + coils PVA (50–150 μM) + coils	37% recurrence rate at 5 y from Kaplan–Meyer estimates (63% treatment free survival) and 4 with surgery performed (85% surgery free) Size > 10 cm predictive of failure requiring surgery
Chatziioannou[88]	2012	10 with 12 AMLs (8 sporadic/2 TS)	8 (5–12)	7 symptomatic 3 asymptomatic	PVA + coils or Embospheres +/− coils	20% recurrence/failure rate at mean f/u of 9 mo with 1 failure needing urgent surgery at 4 d and 1 recurrence needing repeat embolization at 6 mo
Patatas[89]	2013	13 with 13 AMLs (11 sporadic/2 TS)	6.2 (4.2–10)	Not specified (12 performed electively)	Microcoils, Embospheres (500–700 μM), or a combination of both	23% recurrence/ retreatment rate with a median f/u of 46 mo

Abbreviations: AML, angiomyolipoma; PVA, polyvinyl alcohol; TS, tuberous sclerosis.

(odds ratio (OR) 5.88) and risk of pulmonary complications; these complications resulted in the authors advocating for larger sized particles.[34]

Large AMLs (those sized 10 cm or greater) are considered more resistant to RAE. In a series reported by Chan et al, subgroup analysis demonstrated that recurrences necessitating surgery only occurred when treating AMLs > 10 cm in size.[35] Larger tumors are thought to be more difficult to embolize due to their size, multiple feeding vessels, and greater difficultly in isolating them from normal renal parenchyma.

While several series suggest efficacy of treatment of AMLs associated with TS,[36,37] active surveillance of this high-risk group is prudent. In fact, Kothary et al suggest that AMLs treated with RAE in this group may be associated with higher rate of regrowth.[5]

Future Directions

Significant variation in the literature exists for the optimal time from embolization to nephrectomy. In their review of the literature, Kalman and Varenhorst concluded that the optimal delay from embolization to nephrectomy should be less than 48 hours.[9] Postembolization syndrome (characterized by lumbar pain, nausea, and fever) occurs in a majority of patients 1 to 3 days postprocedure, and can be minimized with nephrectomy performed within this timeframe. Additionally, surgery is technically more difficult 72 hours after embolization, which is thought to be secondary to collateral vessel formation.[38] Controversy surrounds the optimal timing of resection; some authors suggest a delay of 24 to 48 hours after embolization, which allows edema to develop facilitating surgical dissection, while other authors have suggested that there should be as minimal delay as possible to prevent collateral vessel formation.[13–15]

Reducing the time between RAE and surgery can minimize postembolization syndrome. In a small series by Lin et al, 8 patients underwent concomitant RAE and surgical resection as compared with 14 control patients who underwent conventional staged preoperative embolization.[39] The concomitant group had no instances of postinfarction syndrome as compared with 36% in the staged group, thereby increasing patient comfort, decreasing hospital stay, and as a result reducing health care costs. Another series by Carvajal et al studied seven patients who underwent concomitant RAE and surgical resection.[40] This study was limited to tumors > 13 cm in size (Stage II, IIIA–B), but did demonstrate safety and increased patient comfort.

Combined Therapies

In treatment of primary hepatic malignancies, there is a growing body of evidence indicating that transarterial embolization therapy in conjunction with localized ablative therapies result in improved patient outcomes as compared with either monotherapy alone.[41–43] The two therapies are thought to be synergistic, with the decreased blood flow from embolization resulting in decreased heat loss during radiofrequency ablation.[44,45] RAE may also serve as a useful adjunctive technique to thermal ablative therapies performed in the setting of nonoperable RCC. The synergistic effect of the two modalities may also have a positive impact on immunomodulatory mechanisms. Li et al combined cryoablation and RAE, and showed a decrease in T-regulatory cells thought to be related to a large volume of cell necrosis and release of tumor antigens.[46] The promotion of T-regulatory cells and inflammation is thought to be one method by which tumor cells can subvert normal immune regulation methods.[47] In clinical practice, the role of RAE in combination with local ablation setting is still largely undefined, with only a few case reports and small series performed demonstrating feasibility and safety.[48–52]

Conclusion

RAE is a safe and effective technique that is well tolerated with few complications, particularly if the time interval from embolization to surgery is reduced to less than 48 hours.

To date, RAE has not been evaluated in a randomized controlled setting, which has contributed to its underutilization. RAE serves as the initial treatment in the management of symptomatic AMLs or those at risk for spontaneous rupture (> 4 cm). In addition, RAE is extremely effective for palliation of symptoms in the setting of nonoperative advanced stage RCC. Potential benefits of this procedure for preoperative RCC treatment include reduction in intraoperative blood loss and operative time by facilitating dissection. Finally, there is suggestion of improved survival benefit after RAE, possibly through immunomodulatory mechanisms. All of these potential benefits warrant the need for prospective studies for further validation.

References

1 Motzer RJ, Agarwal N, Beard C, et al; National Comprehensive Cancer Network. Kidney cancer. J Natl Compr Canc Netw 2011; 9(9):960–977
2 Russo P. The role of surgery in the management of early-stage renal cancer. Hematol Oncol Clin North Am 2011;25(4):737–752
3 Arenson AM, Graham RT, Shaw P, Srigley J, Herschorn S. Angiomyolipoma of the kidney extending into the inferior vena cava: sonographic and CT findings. AJR Am J Roentgenol 1988;151(6): 1159–1161
4 Katabathina VS, Vikram R, Nagar AM, Tamboli P, Menias CO, Prasad SR. Mesenchymal neoplasms of the kidney in adults: imaging spectrum with radiologic-pathologic correlation. Radiographics 2010;30(6):1525–1540
5 Kothary N, Soulen MC, Clark TW, et al. Renal angiomyolipoma: long-term results after arterial embolization. J Vasc Interv Radiol 2005;16(1):45–50
6 Ramon J, Rimon U, Garniek A, et al. Renal angiomyolipoma: long-term results following selective arterial embolization. Eur Urol 2009;55(5):1155–1161
7 Sauk S, Zuckerman DA. Renal artery embolization. Semin Intervent Radiol 2011;28(4):396–406
8 Almgård LE, Slezak P. Treatment of renal adenocarcinoma by embolization: a follow-up of 38 cases. Eur Urol 1977;3(5):279–281
9 Kalman D, Varenhorst E. The role of arterial embolization in renal cell carcinoma. Scand J Urol Nephrol 1999;33(3):162–170

10 Madoff D, Verma R, Ahrar K. Embolotherapy for organ ablation. In: Golzarian J, Sun S, Sharafuddin M, eds. Vascular Embolotherapy. Germany: Springer-Verlag; 2006:201–20
11 Sauk S, Zuckerman DA. Renal artery embolization. Semin Intervent Radiol 2011;28(4):396–406
12 Ginat DT, Saad WE, Turba UC. Transcatheter renal artery embolization: clinical applications and techniques. Tech Vasc Interv Radiol 2009;12(4):224–239
13 Loffroy R, Rao P, Kwak BK, et al. Transcatheter arterial embolization in patients with kidney diseases: an overview of the technical aspects and clinical indications. Korean J Radiol 2010;11(3): 257–268
14 Loffroy R, Rao P, Ota S, Geschwind JF. Renal artery embolisation prior to radical nephrectomy for renal cell carcinoma: when, how and why? Br J Radiol 2010;83(991):630, author reply 631–632
15 Schwartz MJ, Smith EB, Trost DW, Vaughan ED Jr. Renal artery embolization: clinical indications and experience from over 100 cases. BJU Int 2007;99(4):881–886
16 May M, Brookman-Amissah S, Pflanz S, Roigas J, Hoschke B, Kendel F. Pre-operative renal arterial embolisation does not provide survival benefit in patients with radical nephrectomy for renal cell carcinoma. Br J Radiol 2009;82(981):724–731
17 Zielinski H, Szmigielski S, Petrovich Z. Comparison of preoperative embolization followed by radical nephrectomy with radical nephrectomy alone for renal cell carcinoma. Am J Clin Oncol 2000; 23(1):6–12
18 Subramanian VS, Stephenson AJ, Goldfarb DA, Fergany AF, Novick AC, Krishnamurthi V. Utility of preoperative renal artery embolization for management of renal tumors with inferior vena caval thrombi. Urology 2009;74(1):154–159
19 Maxwell NJ, Saleem Amer N, Rogers E, Kiely D, Sweeney P, Brady AP. Renal artery embolisation in the palliative treatment of renal carcinoma. Br J Radiol 2007;80(950):96–102
20 Mukund A, Gamanagatti S. Ethanol ablation of renal cell carcinoma for palliation of symptoms in advanced disease. J Palliat Med 2010; 13(2):117–120
21 Munro NP, Woodhams S, Nawrocki JD, Fletcher MS, Thomas PJ. The role of transarterial embolization in the treatment of renal cell carcinoma. BJU Int 2003;92(3):240–244
22 Onishi T, Oishi Y, Suzuki Y, Asano K. Prognostic evaluation of transcatheter arterial embolization for unresectable renal cell carcinoma with distant metastasis. BJU Int 2001;87(4): 312–315
23 Tigrani VS, Reese DM, Small EJ, Presti JC Jr, Carroll PR. Potential role of nephrectomy in the treatment of metastatic renal cell carcinoma: a retrospective analysis. Urology 2000;55(1):36–40
24 Halpenny D, Snow A, McNeill G, Torreggiani WC. The radiological diagnosis and treatment of renal angiomyolipoma-current status. Clin Radiol 2010;65(2):99–108
25 Oesterling JE, Fishman EK, Goldman SM, Marshall FF. The management of renal angiomyolipoma. J Urol 1986;135(6):1121–1124
26 Soulen MC, Faykus MH Jr, Shlansky-Goldberg RD, Wein AJ, Cope C. Elective embolization for prevention of hemorrhage from renal angiomyolipomas. J Vasc Interv Radiol 1994;5(4):587–591
27 Lee SY, Hsu HH, Chen YC, et al. Evaluation of renal function of angiomyolipoma patients after selective transcatheter arterial embolization. Am J Med Sci 2009;337(2):103–108
28 Boorjian SA, Frank I, Inman B, et al. The role of partial nephrectomy for the management of sporadic renal angiomyolipoma. Urology 2007;70(6):1064–1068
29 Fazeli-Matin S, Novick AC. Nephron-sparing surgery for renal angiomyolipoma. Urology 1998;52(4):577–583
30 Heidenreich A, Hegele A, Varga Z, von Knobloch R, Hofmann R. Nephron-sparing surgery for renal angiomyolipoma. Eur Urol 2002;41(3):267–273
31 Yip SK, Tan PH, Cheng WS, Li MK, Foo KT. Surgical management of angiomyolipoma: nephron-sparing surgery for symptomatic tumour. Scand J Urol Nephrol 2000;34(1):32–35
32 Katsanos K, Sabharwal T, Ahmad F, Dourado R, Adam A. Onyx embolization of sporadic angiomyolipoma. Cardiovasc Intervent Radiol 2009;32(6):1291–1295
33 Lenton J, Kessel D, Watkinson AF. Embolization of renal angiomyolipoma: immediate complications and long-term outcomes. Clin Radiol 2008;63(8):864–870
34 Villalta JD, Sorensen MD, Durack JC, Kerlan RK, Stoller ML. Selective arterial embolization of angiomyolipomas: a comparison of smaller and larger embolic agents. J Urol 2011;186(3):921–927
35 Chan CK, Yu S, Yip S, Lee P. The efficacy, safety and durability of selective renal arterial embolization in treating symptomatic and asymptomatic renal angiomyolipoma. Urology 2011;77(3):642–648
36 Ewalt DH, Diamond N, Rees C, et al. Long-term outcome of transcatheter embolization of renal angiomyolipomas due to tuberous sclerosis complex. J Urol 2005;174(5):1764–1766
37 Williams JM, Racadio JM, Johnson ND, Donnelly LF, Bissler JJ. Embolization of renal angiomyolipomata in patients with tuberous sclerosis complex. Am J Kidney Dis 2006;47(1):95–102
38 Wallace S, Chuang VP, Swanson D, et al. Embolization of renal carcinoma. Radiology 1981;138(3):563–570
39 Lin PH, Terramani TT, Bush RL, Keane TE, Moore RG, Lumsden AB. Concomitant intraoperative renal artery embolization and resection of complex renal carcinoma. J Vasc Surg 2003;38(3):446–450
40 Carvajal R, Orgaz A, Leal JI, et al. Renal embolization and nephrectomy in a single surgical act in high-risk renal tumor pathology. Ann Vasc Surg 2011;25(2):222–228
41 Peng ZW, Zhang YJ, Chen MS, et al. Radiofrequency ablation with or without transcatheter arterial chemoembolization in the treatment of hepatocellular carcinoma: a prospective randomized trial. J Clin Oncol 2013;31(4):426–432
42 Peng ZW, Zhang YJ, Liang HH, Lin XJ, Guo RP, Chen MS. Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial. Radiology 2012;262(2): 689–700
43 Ni JY, Liu SS, Xu LF, Sun HL, Chen YT. Transarterial chemoembolization combined with percutaneous radiofrequency ablation versus TACE and PRFA monotherapy in the treatment for hepatocellular carcinoma: a meta-analysis. J Cancer Res Clin Oncol 2013; 139(4):653–659
44 Peng ZW, Chen MS. Transcatheter arterial chemoembolization combined with radiofrequency ablation for the treatment of hepatocellular carcinoma. Oncology 2013;84(Suppl 1):40–43
45 Rossi S, Garbagnati F, Lencioni R, et al. Percutaneous radio-frequency thermal ablation of nonresectable hepatocellular carcinoma after occlusion of tumor blood supply. Radiology 2000;217(1): 119–126
46 Li Y, Guo Z, Liu CF, et al. Effect of transcatheter renal arterial embolization combined with cryoablation on regulatory CD4+CD25+ T lymphocytes in the peripheral blood of patients with advanced renal carcinoma. Cryobiology 2012;65(1):56–59
47 Finn OJ. Immuno-oncology: understanding the function and dysfunction of the immune system in cancer. Ann Oncol 2012;(23, Suppl 8):6–9
48 Yamakado K, Nakatsuka A, Kobayashi S, et al. Radiofrequency ablation combined with renal arterial embolization for the treatment of unresectable renal cell carcinoma larger than 3.5 cm: initial experience. Cardiovasc Intervent Radiol 2006;29(3): 389–394
49 Arima K, Yamakado K, Kinbara H, Nakatsuka A, Takeda K, Sugimura Y. Percutaneous radiofrequency ablation with transarterial embolization is useful for treatment of stage 1 renal cell carcinoma with surgical risk: results at 2-year mean follow up. Int J Urol 2007; 14(7):585–590, discussion 590
50 Mondshine RT, Owens S, Mondschein JI, Cizman B, Stavropoulos SW, Clark TW. Combination embolization and radiofrequency ablation therapy for renal cell carcinoma in the setting of coexisting arterial disease. J Vasc Interv Radiol 2008;19(4):616–620

51 Woodrum DA, Atwell TD, Farrell MA, Andrews JC, Charboneau JW, Callstrom MR. Role of intraarterial embolization before cryoablation of large renal tumors: a pilot study. J Vasc Interv Radiol 2010; 21(6):930–936

52 Nakasone Y, Kawanaka K, Ikeda O, Tamura Y, Yamashita Y. Sequential combination treatment (arterial embolization and percutaneous radiofrequency ablation) of inoperable renal cell carcinoma: single-center pilot study. Acta Radiol 2012;53(4): 410–414

53 Frasson F, Fugazzola C, Bianchi G, et al. Selective arterial embolization in renal tumors. Radiol Clin (Basel) 1978;47(4):239–251

54 Schulman CC, Struyven J, Giannakopoulos X, Mathieu J. Preoperative embolization of renal tumors—comparison of different methods. Eur Urol 1980;6(3):154–157

55 Frasson F, Roversi RA, Simonetti G, Ziviello M. Embolization of renal tumors. A survey of the Italian experience : 282 patients. Ann Radiol (Paris) 1981;24(5):396–399

56 Giuliani L, Carmignani G, Belgrano E, Puppo P, Quattrini S. Usefulness of preoperative transcatheter embolization in kidney tumors. Urology 1981;17(5):431–434

57 Kato T, Nemoto R, Mori H, Takahashi M, Harada M. Arterial chemoembolization with mitomycin C microcapsules in the treatment of primary or secondary carcinoma of the kidney, liver, bone and intrapelvic organs. Cancer 1981;48(3):674–680

58 Mobilio G, Cavalli A, Bianchi G. Preoperative arterial occlusion in renal tumors: 3 years experience. Int Urol Nephrol 1981;13(1):25–33

59 LeGuillou M, Merland JJ. The indications of embolisation in renal tumor: what remains to be said? Prog Clin Biol Res 1982; 100:603–607

60 Teasdale C, Kirk D, Jeans WD, Penry JB, Tribe CT, Slade N. Arterial embolisation in renal carcinoma: a useful procedure? Br J Urol 1982;54(6):616–619

61 Bono AV, Caresano A. The role of embolization in the treatment of kidney carcinoma. Eur Urol 1983;9(6):334–337

62 Nakano H, Nihira H, Toge T. Treatment of renal cancer patients by transcatheter embolization and its effects on lymphocyte proliferative responses. J Urol 1983;130(1):24–27

63 Ekelund L, Ek A, Forsberg L, et al. Occlusion of renal arterial tumor supply with absolute ethanol. Experience with 20 cases. Acta Radiol Diagn (Stockh) 1984;25(3):195–201

64 Kaisary AV, Williams G, Riddle PR. The role of preoperative embolization in renal cell carcinoma. J Urol 1984;131(4):641–646

65 Kurth KH, Cinqualbre J, Oliver RT, Schulman CC. Embolization and subsequent nephrectomy in metastatic renal cell carcinoma. Prog Clin Biol Res 1984;153:423–436

66 McIvor J, Kaisary AV, Williams G, Grant RW. Tumour infarction after pre-operative embolisation of renal carcinoma. Clin Radiol 1984;35(1):59–64

67 Mebust WK, Weigel JW, Lee KR, Cox GG, Jewell WR, Krishnan EC. Renal cell carcinoma—angioinfarction. J Urol 1984;131(2):231–235

68 Christensen K, Dyreborg U, Andersen JF, Nissen HM. The value of transvascular embolization in the treatment of renal carcinoma. J Urol 1985;133(2):191–193

69 Gottesman JE, Crawford ED, Grossman HB, Scardino P, McCracken JD. Infarction-nephrectomy for metastatic renal carcinoma. Southwest oncology group study. Urology 1985;25(3):248–250

70 Klimberg I, Hunter P, Hawkins IF, Drylie DM, Wajsman Z. Preoperative angioinfarction of localized renal cell carcinoma using absolute ethanol. J Urol 1985;133(1):21–24

71 Lammer J, Justich E, Schreyer H, Pettek R. Complications of renal tumor embolization. Cardiovasc Intervent Radiol 1985;8(1):31–35

72 Leinonen A. Embolization of renal carcinoma. Comparison between the early results of Gelfoam and absolute ethanol embolization. Ann Clin Res 1985;17(6):299–305

73 Weigel JW, Mebust WK, Foret JD, et al. Treatment of renal cell carcinoma with renal infarction, delayed nephrectomy, medroxyprogesterone, and xenogeneic immune RNA. Urology 1985; 25(2):103–105

74 Chudácek Z, Zavázal V. Palliative embolization of renal tumors. I. Immunologic reaction to the embolization. Radiol Diagn (Berl) 1986;27(2):211–213

75 Karwowski A, Wojtowicz J. Long-term results of embolization in renal tumors. Radiol Diagn (Berl) 1987;28(4):533–535

76 Kurth KH, Debruyne FM, Hall RR, et al. Embolization and postinfarction nephrectomy in patients with primary metastatic renal adenocarcinoma. Eur Urol 1987;13(4):251–255

77 Nurmi M, Satokari K, Puntala P. Renal artery embolization in the palliative treatment of renal adenocarcinoma. Scand J Urol Nephrol 1987;21(2):93–96

78 Stoesslein F, Schwenke A, Muenster W. Percutaneous transluminal embolization for improved prognosis of renal cell carcinoma—dependence on tumor stages. Cardiovasc Intervent Radiol 1988; 11(2):91–96

79 Swanson DA, Wallace S. Surgery of metastatic renal cell carcinoma and use of renal infarction. Semin Surg Oncol 1988;4(2):124–128

80 Kato T, Sato K, Abe R, Moriyama M. The role of embolization/chemoembolization in the treatment of renal cell carcinoma. Prog Clin Biol Res 1989;303:697–705

81 Lanigan D, Jurriaans E, Hammonds JC, Wells IP, Choa RG. The current status of embolization in renal cell carcinoma—a survey of local and national practice. Clin Radiol 1992;46(3):176–178

82 Bakal CW, Cynamon J, Lakritz PS, Sprayregen S. Value of preoperative renal artery embolization in reducing blood transfusion requirements during nephrectomy for renal cell carcinoma. J Vasc Interv Radiol 1993;4(6):727–731

83 Park JH, Kim SH, Han JK, Chung JW, Han MC. Transcatheter arterial embolization of unresectable renal cell carcinoma with a mixture of ethanol and iodized oil. Cardiovasc Intervent Radiol 1994;17(6): 323–327

84 Chick CM, Tan BS, Cheng C, et al. Long-term follow-up of the treatment of renal angiomyolipomas after selective arterial embolization with alcohol. BJU Int 2010;105(3):390–394

85 Lee SY, Hsu HH, Chen YC, et al. Embolization of renal angiomyolipomas: short-term and long-term outcomes, complications, and tumor shrinkage. Cardiovasc Intervent Radiol 2009;32(6): 1171–1178

86 Takebayashi S, Horikawa A, Arai M, Iso S, Noguchi K. Transarterial ethanol ablation for sporadic and non-hemorrhaging angiomyolipoma in the kidney. Eur J Radiol 2009;72(1):139–145

87 Bishay VL, Crino PB, Wein AJ, et al. Embolization of giant renal angiomyolipomas: technique and results. J Vasc Interv Radiol 2010;21(1):67–72

88 Chatziioannou A, Gargas D, Malagari K, et al. Transcatheter arterial embolization as therapy of renal angiomyolipomas: the evolution in 15 years of experience. Eur J Radiol 2012;81(9):2308–2312

89 Patatas K, Robinson GJ, Ettles DF, Lakshminarayan R. Patterns of renal angiomyolipoma regression post embolisation on medium- to long-term follow-up. Br J Radiol 2013;86(1024):20120633