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The Role of Transarterial Embolization in the Treatment of Renal Tumors

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A – research concept and design; **B** – collection and/or assembly of data; **C** – data analysis and interpretation; **D** – writing the article; **E** – critical revision of the article; **F** – final approval of article

Abstract

Background. Renal arterial embolization (RAE) is one of the adjunctive methods in the treatment of renal tumors. Embolization is performed in patients prior to nephrectomy, in patients with inoperable renal tumors as palliative treatment.
Objectives. The purpose of the study was to present and to analyze our own experiences in the embolization of renal tumors.
Material and Methods. A retrospective analysis of 33 patients treated using RAE between 2011 and 2013 was carried out. In 30 cases (91%), embolization was performed due to renal carcinoma and in 3 cases (9%) due to angiomyolipoma. In 11 patients intervention was performed as a palliative procedure because of advanced disease. Histoacrylic glue, polyvinyl alcohol, sponge pledgets and embolization coils were used for embolization.
Results. In 20 patients (61%), selective RAE was performed, whereas superselective RAE was carried out in 13 patients (39%). The technical success rate of RAE was 100%. In one case the procedure was complicated by reflux of the histoacrylic glue into the common femoral artery with its embolization that required surgical embolectomy. We used histoacrylic glue in 26 embolizations (79%), in 19 procedures (58%) as the only embolization agent. Polyvinyl alcohol was used in 10 procedures (30%), gelatin sponge pledgets and absolute ethanol in 6 patients (18%). In 4 cases (12%), coils were implemented. In 22 patients (67%), one or more components of postembolization syndrome (PES) developed. In all 22 patients with PES (100%), severe lumbar pain was observed and administration of analgesics proved necessary. In 10 patients treated by palliative embolization, both a regression of macrohaematuria and an increase in hemoglobin level were observed. In 10 further patients, the creatinine level decreased following RAE.
Conclusions. RAE is an effective and minimally-invasive intervention burdened with low risk of major complications. PES occurs in about two-third of patients. In the majority of patients after palliative embolization, haematuria decreases and the quality of life improves (**Adv Clin Exp Med 2015, 24, 5, 837–843**).

Key words: kidney neoplasms, embolization, endovascular procedures, cyanoacrylate glue, coils.

Renal carcinoma (RC) accounts for 2–3% of all malignancies and is the sixth most common malignancy in males and the 9th most common malignancy among females. It develops most commonly asymptomatically, however, in 40–60% of patients haematuria appears, which can be the first and the only symptom. Advanced RC may cause flank pain, hypogastric pain, epigastric gripping pain, lower leg swelling and systemic symptoms (weight loss, cachexia, fever). Independent of the stage of the cancer, surgery remains the most relevant modality of treatment. In all patients, efforts are aimed at resection of the primary tumor and potential resectable metastatic tumors. Radiotherapy is implemented rarely and only to control pain intensity in patients with bone metastases. Embolization of

bone metastases performed for similar reasons as in radiotherapy have been reported [1, 2]. Systemic treatment is implemented in patients with generalized disease. Visceral embolization is performed in rare cases [3].

The procedure of embolization involves insertion of a vascular catheter and its X-ray guided placement in a target vessel followed by administration of embolization material that result in vessel occlusion, focal ischemia or acute renal infarction. Indications for embolization of renal tumors include haematuria, pain, presurgical reduction of tumor mass (cytoreductive embolization), no consent of the patient for the surgery, anesthesiological contraindications and advanced neoplastic disease (palliative embolization) [4].

Material and Methods

Renal arterial embolization was performed in 33 patients (17 females and 16 males) treated at our institution between 2011 and 2013. Median patient age was 64 (age range 32–83). A retrospective analysis of laboratory data, clinical findings and outcomes of the embolization procedures was carried out. In most of the patients (n = 30; 91%), embolization was performed due to RC, and in the remaining 3 patients (9%) due to angiomyolipoma (AML). Two patients underwent the procedure of RAE twice. In 11 cases the intervention was performed as a palliative procedure because of advanced malignancy. Metastatic foci were observed most commonly in lungs – in 9 patients with metastatic RC (82%).

In all cases, multiphase computed tomography (CT) including arterial phase was carried out as the initial cross-sectional imaging modality not only for the purpose of tumor staging but to identify the arterial supply of the renal tumors. In patients with RC, it was the baseline study performed for tumor staging. In all cases, the initial abdominal CT was used to identify both arterial supply of the tumors and potential anatomical variants of the renal arteries prior to RAE.

Vascular access was obtained for all the embolization procedures. A vascular sheath (sized 6-7F) was introduced *via* the common femoral artery and its tip was located directly caudally to the origin of the renal arteries. Next, the renal artery was selectively catheterized with the use of a 4-5F catheter. In the case of superselective embolizations, a 2.2-2.7F microcatheter was additionally used. The most commonly used embolization material was a mixture of n-butyl-2-cyanoacrylate (NBCA) glue (Histoacryl; B. Brown, Melsungen, Germany) and an oil iodinated contrast medium (Lipiodol® UltraFluide; Guerbet, USA*)* in a concentration of 17–25%. We used NBCA in 26 embolizations (79%), in 19 procedures (58%) as the only embolization agent. In 5 patients (15%), both histoacrylic glue and polyvinyl alcohol particles (diameter 100–1000 μm) were applied. In one case (3%) NBCA was used in combination with gelatin sponge pledgets and absolute ethanol, and in one other patient (3%) NBCA was used with absolute ethanol. Polyvinyl alcohol was used in 10 procedures (30%), gelatin sponge pledgets and absolute ethanol in 6 patients (18%), and in 4 cases (12%) McRay coils (3–6 mm) were implemented.

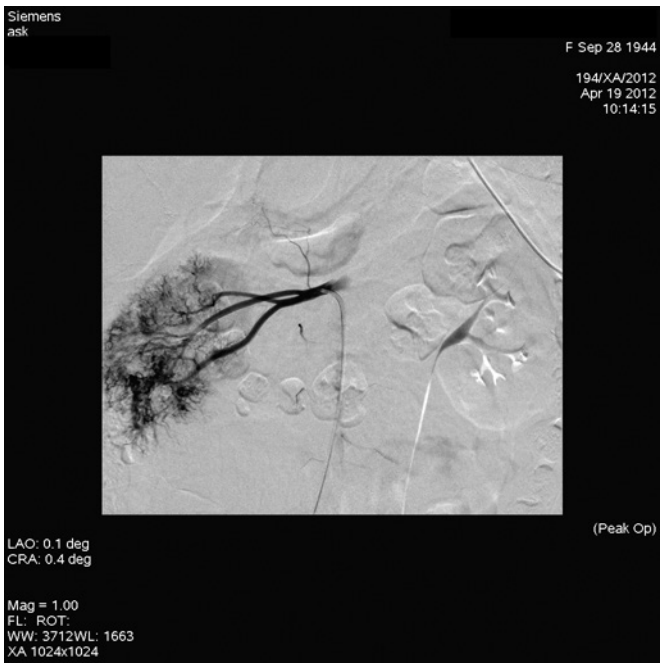

Fig. 1A. Selective digital subtraction angiography in patient with renal cell carcinoma of right kidney. A. Preinterventional angiography *via* MP catheter placed in the right renal artery demonstrating hypervascular tumor of the right kidney. Rich mesh of pathological arterial branches can be seen

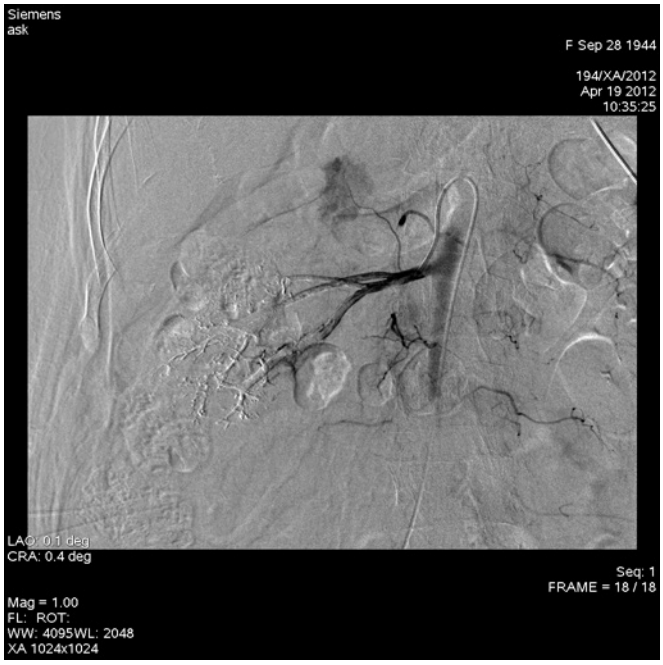

Fig. 1B. Postembolization angiography *via* Sim catheter showing complete occlusion of arterial vessels of the right kidney with histoacrylic glue. More cranially, hypervascular metastatic lesion in the right suprarenal gland still strongly opacifies while renal parenchyma shows no opacification

Results

In 20 patients (61%), selective embolization of either renal artery was performed, whereas superselective RAE was carried out in 13 patients (39%). Two patients underwent a two-step procedure. In 3 cases (9%) lumbar artery embolization was additionally performed, in 1 case (3%) suprarenal artery embolization and in another case (3%) capsular artery embolization was carried out. Technical success of the embolization procedure was achieved in all of the patients (100%). In one patient, however, the procedure was complicated by reflux of the histoacrylic glue into the right common femoral artery (CFA) with its subsequent acute embolization and occlusion, which required emergency surgical intervention. Embolectomy of the CFA was performed and the arterial flow was restored.

In 22 patients (67%), one or more components of transient PES developed, which constituted a systemic reaction to embolic agents and local postembolization circulation disorders, resulting in total or partial renal infarction and subsequent necrosis. Postembolization syndrome presented in the studied group 1–3 days following the intervention and subsided after maximally 6 days without permanent consequences. The symptoms of PES included lumbar pain, fever, nausea and vomiting.

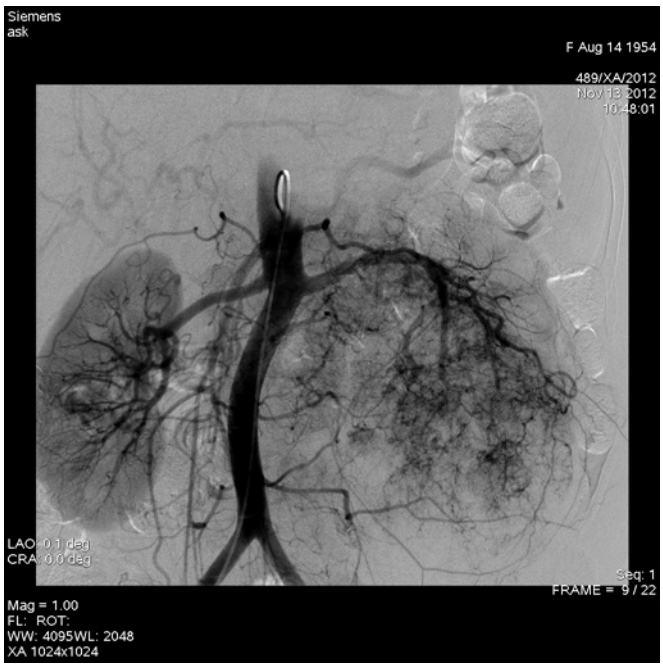

Fig. 2A. Non-selective digital subtraction angiography in patient with giant renal cell carcinoma of left kidney. Tip of pig-tail catheter located in suprarenal portion of abdominal aorta. A. Preinterventional angiogram of abdominal aorta and its visceral branches reveals a giant hypervascular tumor originating from the left kidney and displacing abdominal aorta onto the right

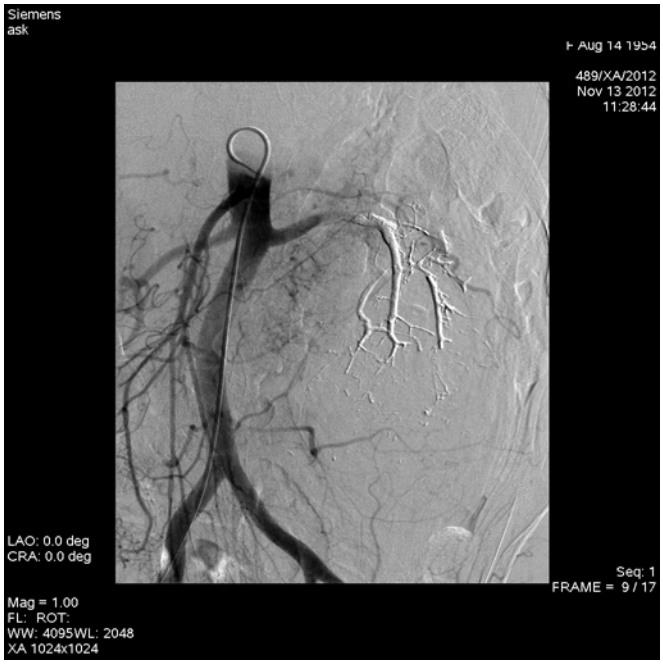

Fig. 2B. Postembolization angiogram demonstrates complete occlusion of branches of the left renal artery with histoacrylic glue

In all 22 patients with PES (100%), severe lumbar pain was observed and administration of analgesics proved necessary. In order to control the pain, non-steroidal anti-inflammatory drugs (NSAID) (n = 2; 9%), weak and moderate opiates (n = 19; 86%) and eventually strong opiates (n = 1; 5%) were administered. The pain subsided after drug administration, in most cases, 3 days after the procedure. In 15 patients with PES (68%), fever was observed (range: 37.6–40.6; median 38.6). Paracetamol was used to reduce fever. In one patient, diarrhea was noted, and 4 further patients presented with nausea and vomiting that subsided after administration of analgesics and metoclopramide. Additionally, in 6 patients (18%) with urine retention, short-term bladder catheterization was necessary.

In 10 patients with RC treated by palliative transarterial embolization (91%), partial or complete regression of macrohaematuria was observed and laboratory exams demonstrated an increase in hemoglobin level by 0.5 to 4.1 g/dL (median 1.4 g/dL). In 10 patients following embolization (30%), the creatinine level decreased by 0.04 to 1.51 mg/dL (median 0.32 mg/dL), which can be assumed to be an indicator of improvement in renal filtration. The potassium level decreased in 12 patients (36%) (range: 0.21–1.27 mmol/L; average: 0.66 mmol/L)

Discussion

Therapeutic transarterial embolization of renal arteries was first mentioned in 1969. The procedure was experimentally performed on dogs by Lalli et al. [5]. Almgard et al., in 1973, performed embolization in a group of 19 human patients with advanced metastatic disease [6]. Next, in half of the patients, radical nephrectomy was performed and, according to the authors, the procedure was facilitated due to previous transarterial embolization. Since then the procedure has been commonly applied in humans. Development of the instrumentation of interventional radiology, advancement of imaging modalities, and easier access to and improvement in the quality of embolization agents have become valuable supplements to the complex treatment of renal tumors [4]. Both palliative and presurgical embolizations constitute effective methods in reducing haematuria and pain. According to some authors, presurgical embolization significantly reduces loss of blood during surgery; however it does not influence the general survival of patients with RCC [7].

At our institution, embolization was performed as a method of palliative treatment in 33% of cases (n = 11), whereas in the remaining 67% of patients, it was followed by nephrectomy. A similar application of the embolization procedure was demonstrated by Vaicekavicius et al., who used embolization as palliative management in 28% of cases, in 72% prior to nephrectomy. [8] Schwartz et al. reported a similar percentage (66%) of cytoreductive embolizations [9]. According to most other authors, the interventions were performed exclusively as a palliative procedure [10, 11]. Embolization effectively reduced the incidence and intensity of haematuria, which resulted in an increase in hemoglobin level in 10 out of 11 patients who had undergone palliative embolization (91%) and there was no further necessity to administer blood derivate products in these patients. In a report by Maxwell et al., an increase in hemoglobin level was noted in all of the patients [12].

In our study, selective embolization of either renal artery was performed in 20 patients (61%), whereas superselective embolization of the branches of the renal artery was performed in 13 patients (39%). Vaicekavicius et al. performed selective embolization in 93% of patients and the superselective procedure was done in 7% [8]. Superselective embolization is a good method of treatment for small tumors, allows for reduction of iatrogenic necrosis while sparing normal renal parenchyma. However, Guy et al. demonstrated the recurrence of micro- or macrohaematuria only in patients following superselective embolization [13].

The mixture of n-butyl-2-cyanoacrylate (NBCA) glue (Histoacryl; B. Brown, Melsungen, Germany) and oil iodinated contrast medium (Lipiodol® UltraFluide; Guerbet, USA) was the most commonly used embolization material in our patients. We used cyanoacrylate glue in 26 embolizations (79%). Polyvinyl alcohol (PVA) was applied in 10 procedures (30%), gelatin sponge pledgets and absolute ethanol in 18% of patients and McRay coils were used in 12% of cases. The high rate of administration of cyanoacrylate glue results from our experience with the application of glue acquired when treating various vascular malformations. In the available literature, there is no one preferred embolization agent. Combined methods are often applied that vary depending on the institution. Guy et al. used PVA in 45% of patients, PVA combined with gelatin sponge in 15%, PVA combined with coils in 15% and gelatin sponge with coils in 20% [13]. Schwartz et al. most commonly used coils (87%) [9]. Polyvinyl alcohol, absolute ethanol and gelatin sponge were also used. Onishi et al. applied only ethanol in a group of patients with RCC [14]. Munro et al. most often used ethanol combined with other agents (alcohol with coils in 85%, alcohol and gelatin sponge in 8%, in 7% only alcohol) [10]. May et al. applied only coils in 95% of 227 presurgical renal transarterial embolizations [7].

In all cases, initial abdominal multiphase CT made it possible to identify both the arterial supply of the tumors and to detect anatomical variants of the renal arteries embracing the site of origin of the renal artery, duplication, triplication or early division of the renal artery [15]. Identification of the anatomical variants of the renal artery was relevant because of its impact on the embolization procedure and typically necessitated the embolization of accessory ipsilateral renal artery.

The most common complication of the embolization procedure is a group of symptoms called postembolization syndrome. It includes lumbar pain, fever, nausea, vomiting and diarrhea. In our material, one or more components of transient PES developed in 22 patients (67%). Severe lumbar pain was observed in all the patients with PES and administration of analgesics was necessary. Non-steroidal anti-inflammatory drugs (ketoprofen) (n = 2; 9%), weak opiates (tramadol) (n = 4; 18%), moderate opiates (pethidine) (n = 19; 86%) and strong opiates (morphine) (n = 1; 5%) were administered in order to control the pain. The pain subsided after drug administration, in most cases 3 days after the procedure. In 15 patients with PES (68%) fever was observed (temperature range: 37.6–40.6; median 38.6). Paracetamol (acetaminophen) was used to reduce fever. One patient presented with diarrhea and 4 further patients required administration of metoclopramide (due to nausea and vomiting).

According to the literature, the incidence of PES ranges widely from 40% to nearly 90% of patients. The lowest rate of PES is reported by Maxwell et al. [12]. In their material, lumbar pain was observed in 42% of patients, however only 5% required administration of analgesics; fever occurred in 26% of patients, nausea and vomiting in 10% of patients. Guy et al. reported manifestations of postembolization syndrome in 60% of patients and fever in 40% [13]. Schwartz et al. reported the incidence rate of PES to be 74.4%, which is similar to that in our material; according to their report, lumbar pain was observed in 61.1%, fever in 37.2%, nausea in 24% and vomiting in 9.1% of patients [9]. The symptoms were controlled using analgesics and antiemetic drugs. Other authors observed the symptoms of PES in over 80% of patients [8, 14]. May et al. analyzed 227 embolization procedures and observed PES in 89% of cases with a predominance of pain (100%) and fever (49%) [7].

Other authors reported, similarly to our observations, that the symptoms resolved 2–3 days after the procedure, typically after administration of analgesics, antipyretic and antiemetic drugs. Unintentional embolization of the common femoral artery was a consequence of a technical mistake. The authors suggest that embolization using glue should be performed using coaxial catheters with a "mother" catheter placed in the lumen of the renal artery during the procedure.

Regarding tumor histopathology, we demonstrated a predominance of renal cell carcinoma (RCC) (91%) followed by AML (9%). Also according to other authors, embolization was most commonly performed due to RCC: in 100% [13, 14], 90% [12], 88% [16] and 74% [9]. Embolization of the AML was carried out in the case of clinically symptomatic tumors – in patients with its rupture or impending rupture, and at times RAE was performed because of the large size of the tumor [17].

Embolization of other rare renal malignancies, like sarcomas, is also reported [4].

Some authors report on the immunological benefits in patients undergoing embolization prior to nephrectomy [18, 19]. An increase in activity of NK lymphocytes was demonstrated in the first 24 h post--embolization. Extensive post-embolization tumor necrosis stimulates the immunological system. An increase in time between tumor embolization and surgery means the patient receives a specific immunotherapy "self-vaccination". The hypothesis that embolization can stimulate the production of anti-cancer antibodies is highly probable, but this still needs to be confirmed in larger series [20].

Embolization is a simple and short procedure that is an important alternative to operative treatment of renal tumors. Embolization is mainly applied as a cytoreductive and palliative procedure in the treatment of the advanced stage RC, which alleviates symptoms like pain and haematuria. The procedure is also applied as a preoperative intervention, prior to elective nephrectomy, which is aimed at a reduction of loss of blood during the resections of large highly-vascularized tumors [7, 9, 12, 13]. Onishi et al. demonstrated an improvement in the quality of life and non-significant prolonged survival in patients with inoperable metastatic renal cancer who had undergone embolization [14].

Subramanian et al. performed a retrospective analysis in a group of patients for radical nephrectomy and inferior vena cava thrombectomy which demonstrated negative impact of presurgical embolization on outcomes of the surgery when compared to the non-embolization subgroup [21]. The outcomes of retrospective analyses are at times inconsistent and there are no prospective randomized trials that would compare the surgical parameters between embolization and non-embolization subgroups.

Therefore, as a result of only little reliable data, the European Society of Urology does not recommend applying this method of treatment as a routine adjunct management in patients prior to nephrectomy due to renal cancer and reserves the procedure for patients with non-resectable tumors and in order to reduce blood-loss during resection of hypervascular bone metastases [3].

The authors concluded that renal arterial embolization is an effective and safe minimally-invasive intervention burdened with a low risk of severe complications. Postembolization syndrome occurs in about two-thirds of patients, at times it requires short-term administration of opiates and usually subsides 3 days after the procedure. In the majority of patients after palliative embolization, haematuria decreases and the quality of life improves.

References

[1] **Chatziioannou AN, Johnson ME, Pneumaticos SG, Lawrence DD, Carrasco CH:** Preoperative embolization of bone metastases from renal cell carcinoma. Eur Radiol 2000, 10, 593–596.

[2] **Basile A, Rand T, Lomoschitz F, Toma C, Lupattelli T, Kettenbach J, Lammer J:** Trisacryl gelatin microspheres versus polyvinyl alcohol particles in the preoperative embolization of bone neoplasms. Cardiovasc Intervent Radiol 2004, 27, 495–502.

[3] **Ljungberg B, Cowan NC, Hanbury DC, Hora M, Kuczyk MA, Merseburger AS, Patard JJ, Mulders PF, Sinescu IC:** European Association of Urology Guideline Group. EAU Guidelines on renal cell carcinoma: The 2010 Update. Eur Urol 2010, 58, 398–406.

[4] **Ward JF, Velling TE:** Transcatheter therapeutic embolization of genitourinary pathology. Rev Urol 2000, 2, 236–252.

[5] **Lalli AF, Peterson N, Bookstein JJ:** Roentgen-guided infarctions of kidney and lungs: a potential therapeutic technique. Radiology 1969, 93, 434–435.

[6] **Almgard LE, Fernström I, Haverling M, Ljungqvist A:** Treatment of renal adenocarcinoma by embolic occlusion of the renal circulation. Br J Urol 1973, 45, 474–479.

[7] **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, 724–731.

[8] **Vaicekavicius E, Pranculis A:** Transcatheter renal arterial embolization in malignant renal neoplasms: clinical results and indications for use of the method in multi-profile hospitals. Medicina (Kaunas) 2002, 38, 888–891.

[9] **Schwartz MJ, Smith EB, Trost DW, Vaughan Jr. ED:** Renal artery embolization: clinical indications and experience from over 100 cases. BJU Int 2007, 99, 881–886.

[10] **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, 240–244.

[11] **Gallucci M, Guaglianone S, Carpanese L, Papalia R, Simone G, Forestiere E, Leonardo C:** Superselective embolization as first step of laparoscopic partial nephrectomy. Urology 2007, 69, 642–645.

[12] **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, 96–102. Erratum in: Br J Radiol 2007, 80, 853.

[13] **Guy L, Alfidja AT, Chabrot P, Ravel A, Boiteux JP, Boyer L:** Palliative transarterial embolization of renal tumors in 20 patients. Int Urol Nephrol 2007, 39, 47–50.

[14] 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, 312–315.
[15] Kurcz J, Nienartowicz E, Słonina J, Garcarek J, Moroń K: The usefulness of CT-angiography in detecting anatomical variants of arteries arising from the abdominal aorta and aortic arch. Adv Clin Exp Med 2007, 16, 751–760.
[16] Jae Hyung P, Woo Sun K, Man Chung H, Chong W: Renal Arterial Embolization with Absolute Ethanol. J Korean Med Sci 1987, 2, 13–18.
[17] Davis C, Boyett T, Caridi J: Renal Artery Embolization: Application and Success in Patients with Renal Cell Carcinoma and Angiomyolipoma. Semin Intervent Radiol 2007, 24, 111–116.
[18] Bakke A, Gothlin JH, Haukaas SA, Kalland T: Augmentation of natural killer cell activity after arterial embolization of renal carcinomas. Cancer Res 1982, 42, 3880–3883.
[19] 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, 24–27.
[20] Kalman D, Varenhorst E: The role of arterial embolization in renal cell carcinoma. Scand J Urol Nephrol 1999, 33, 162–170.
[21] 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 cava thrombi*. Urology 2009, 74, 154–159.

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