



Palliative embolization of renal tumors

Palijativna embolizacija tumora bubrega

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Abstract

Background/Aim. Palliative embolization of renal tumors is the method of choice in the treatment of advanced inoperable renal cell carcinoma in patients with hematuria and pain. Patients with small tumors in the remaining solitary kidney who refuse surgery are suitable for this type of therapy as well as patients with centrally located inoperable tumors. The prerequisite for successful capillary embolization is the closure of the main arterial trunk with metal spirals. **Methods.** In the period from 2000 to 2010 we conducted 42 palliative embolizations. The average age of the patients was 75 years, including 26 men and 16 women. In 8 of the patients the intervention was repeated and in one with severe AV shunts embolization was performed 4 times. Embolization was performed with alcohol, Ivalon 150–250 μm and with metal coils. **Results.** No serious complications were observed during and after the intervention. Fourteen patient were still alive then and among the deceased patients the average survival time was 13.5 ± 10.8 months with the range of 1 to 56 months. The minimal survival time was 1 month with a maximum survival time of 56 months. **Conclusion.** Our results are consistent with data in the literature. Survival in patients without metastases was longer than in those with metastases, as confirmed by the 14 of the patients from the study. An additional therapeutic safety in the treatment of small cancers is provided with a combination therapy of embolization and radiofrequency thermoablation.

Key words:

kidney neoplasms; carcinoma, renal cell; hematuria; palliative care; embolization, therapeutic; radiography, interventional.

Apstrakt

Uvod/Cilj. Palijativna embolizacija tumora bubrega je metoda izbora u lečenju uznapredovalih inoperabilnih karcinoma bubrega kod bolesnika sa hematurijom i bolovima. Bolesnici sa malim tumorom na preostalom bubregu su pogodni za ovaj vid terapije, ukoliko ti bolesnici odbijaju operativni zahvat ili ukoliko tumor leži centralno, tako da operativna enukleacija nije moguća. Preduslov za uspešnu embolizaciju je kapilarna embolizacija, a glavno arterijsko stablo se zatvori metalnim spiralama. **Metode.** U periodu 2000–2010 godine kod 42 bolesnika urađena je palijativna embolizacija. Prosečna starost bolesnika iznosila je 75 godina. U studiju je bilo uključeno 16 žena i 26 muškaraca. Kod 8 bolesnika intervencija je ponovljena, a kod jednog, sa izraženim AV-šantovima, embolizacija je urađena četiri puta. Embolizacija je rađena alkoholom, Ivalonom 150–250 μm i metalnim spiralama. **Rezultati.** U toku intervencije i nakon intervencije nije bilo teških komplikacija. Ukupno 14 bolesnika još su živi, a kod umrlih prosečno preživljavanje iznosilo je $13,5 \pm 10,8$ meseci. Minimalno preživljavanje iznosilo je jedan mesec, a maksimalno 56 meseci. **Zaključak.** Naši rezultati podudaraju se sa podacima iz literature. Preživljavanje kod bolesnika bez metastaza duže je nego kod bolesnika sa metastazama, što potvrđuje i 14 bolesnika iz naše studije. Dodatnu sigurnost u terapiji malih karcinoma pruža kombinovana terapija: embolizacija i radiofrekventna termoablacija.

Ključne reči:

bubreg, neoplazme; hipernefrom; hematurija; lečenje, palijativno; embolizacija, terapijska; radiografija, interventna.

Introduction

Renal cell carcinoma is a rare tumor which accounts for 1.2–3% of all newly diagnosed cancers. Men are afflicted twice as often as women. It usually occurs between the 5th and the 7th decade of life. Renal cell carcinoma is the third most common cancer in the field of urology following bladder cancer and prostate can-

cer. The therapy of choice is nephrectomy or enucleation surgery of smaller tumors if feasible, depending on tumor location.

Percutaneous transarterial embolization of the kidney is a minimally invasive therapeutic procedure by which complete or partial radiological nephrectomy can be performed.

Percutaneous renal embolization was first performed experimentally on animals in 1969 by Lalli et al.¹ In 1973

Almgard et al.² reported embolization of a patient with renal cell carcinoma.

Since then, not only the embolization technique has changed, but also the diagnosis of renal cell carcinoma was revolutionized by the introduction of computed tomography (CT) and magnetic resonance imaging (MRI). Palliative embolization is the treatment of choice for patients with advanced kidney cancer in whom surgery is technically unfeasible or if they have a high surgical risk. The main indication for the implementation of embolization in these patients is hematuria, which can be treated successfully with this method regarding aspects of technique and clinical outcome. Furthermore these patients often have severe pain because of the infiltration of the organ as well as the surrounding anatomical structures, in which case embolization is also an adequate paintherapy. Metastases are not a contraindication to implementing this procedure regarding the two above mentioned indications.

In asymptomatic patients without distant metastases the complete necrosis of the tumor is achieved by capillary embolization so that a portion of these patients are converted from the inoperable to the operable status.

Another indication for palliative embolization is a small tumor in the remaining solitary kidney in which partial resection of the kidney is not technically possible or in patients who refuse surgery on the remaining kidney.

Patients with advanced metastases and small tumors of the kidney are also indications for embolization. Embolization is performed on the capillary level. For capillary embolization alcohol (96%), Ethibloc and polyvinyl alcohol foam – Ivalon (150–250 µm) are used. Alcohol is the cheapest and most efficient embolization agent. The disadvantage of using alcohol as the only agent to embolize is that it must be applied to a blocked blood vessel in order to prevent reflux or otherwise must be made visible so as to be able to make sure, that reflux can be seen.

After capillary embolization is completed, the occlusion of the central main stem of the renal artery is performed by using spirals.

Methods

This study included 42 patients in whom palliative embolizations of renal tumors were performed in the period from 2000 to 2010. The average age of patients was 75 years, including 26 men and 16 women. Indications for embolization were as follows: inoperability demonstrated by CT or MRI, surgery contraindicated due to poor general health status, surgery refusal, tumors in both kidneys, and tumor in the remaining kidney after unilateral nephrectomy.

All the patients were diagnosed by CT scan or MRI. CT examinations were biphasic with a portal venous phase after 65 sec and an urographic phase after 10 min. As contrast agent we used Xenetix 350. The contrast medium was applied by using an injector with a flow rate of 3.5 mL/sec.

MRI was performed with T2 and T1 sequences without contrast agent and after the contrast agent (Dotarem[®]) had been injected manually in a quantity according to the patients weight (0.1 mg/kg). After administration of the contrast me-

dium the T1 sequence with fat suppression (T1 VIBE) was done to make it easier to recognize the contrast discoloration of pathological structures.

After selective angiography has been performed, the embolization procedure follows. Embolization was done at the first capillary level. The embolic materials used in this study at the capillary level were alcohol or Ivalon[®] (150–250 µm particles).

For the intervention 96% alcohol was used. In the beginning of the study the alcohol embolization was done by balloon occlusion using latex balloons. In the second half of the study 1/3 of lipiodol was added (to alcohol so as to make it visible), as occluding catheters were not available anymore. Some patients underwent combined embolization with alcohol and Ivalon[®] – the so-called “sandwich” technique. The advantage of using Ivalon[®] is that the supplying blood vessel need not to be blocked. Upon completion of capillary embolization, control angiography was performed. If renal tumor is sufficiently embolized, central embolization of the major supplying vessel (inlet vessel) should be done using metal coils. In the study, Tornado[®] spirals provided by Cook Medical were used.

After having embolized the tumor on the capillary and more central level, aortography was performed to confirm the complete embolization and to show the state of the surrounding non-targeted blood vessels.

Results

The major symptoms that lead the patients to their physicians are shown in Table 1.

Table 1
The major symptoms and radiological findings in the studied patients

| Parameter | Patients, n = 42 (100%) | |
|--|-------------------------|--------|
| | n (%) | |
| Symptoms | | |
| pain | 13 | (31,0) |
| hematuria | 16 | (38,1) |
| weight loss > 5 kg | 18 | (42,9) |
| Radiological findings | | |
| vein infiltration | 5 | (11,9) |
| necrosis | 30 | (71,4) |
| infiltration of the surrounding organs | 6 | (14,3) |

One of the patients was diagnosed with bilateral tumors, so unilateral nephrectomy was done and superselective embolization was performed on the remaining kidney.

In 7 of the patients after nephrectomy tumor was discovered in the remaining kidney. Some of these patients refused surgery or the tumor had the central location, making partial nephrectomy impossible.

Angiographic findings of small residual tumor on the right kidney before and after embolization as well as CT scan after a year are shown in Figure 1.

The mean tumor size was 7.35 cm. The smallest tumor measured 2 cm and the largest measured 15 cm. There were 11 tumors found in the left kidney and 31 tumors in the right kidney. Radiologic findings are shown in Table 1.

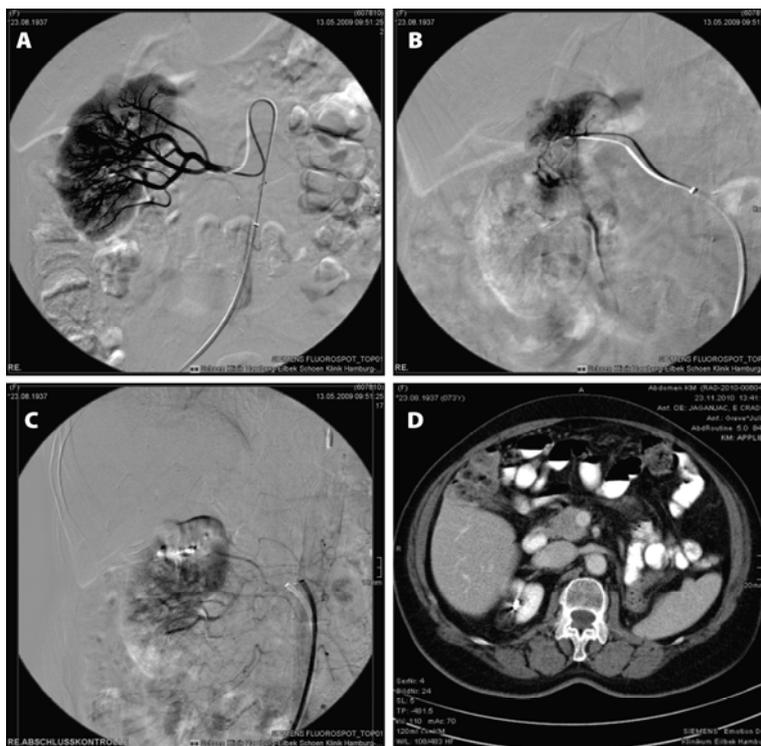


Fig. 1 – Small residual tumor on the right kidney: a) and b) – angiographic findings; c) angiographic finding after embolization; d) computed tomography scan after a year showing scar tissue in the kidney.

Lymph node metastases were present in 10 patients and 11 patients had distant metastases. Two of the patients had infiltration of the hollow system.

In 8 of the patients embolization was repeated, and in

one it was repeated 3 times, due to severe AV shunts.

Metastatic tumor of the left kidney and CT of lung showing metastases, and angiographic findings before and after embolization are shown in Figure 2.

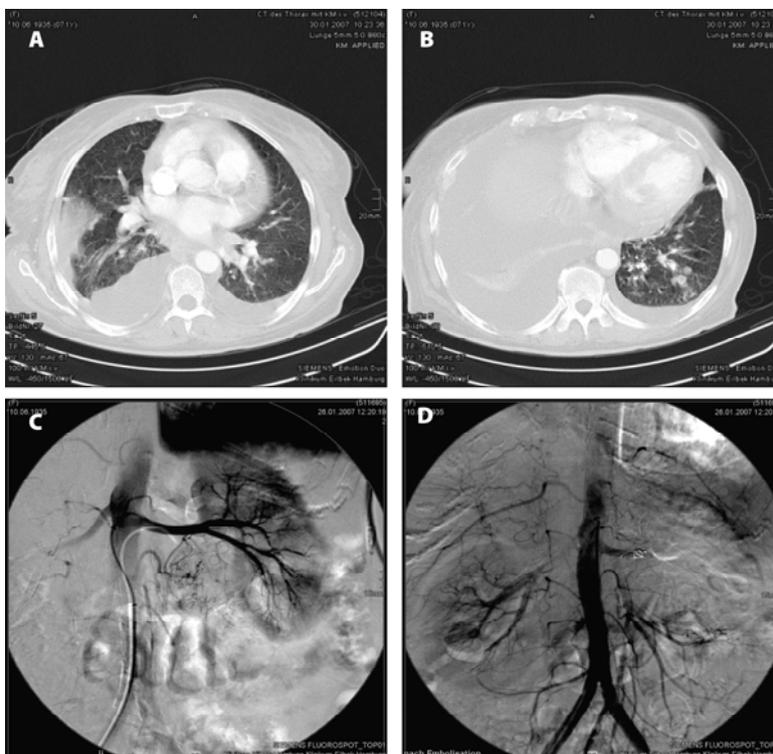


Fig. 2 – Metastatic tumor of the left kidney: a) and b) – computed tomography scan of lung showing metastases; c) angiographic finding before, and d) angiographic finding after embolization.

After intervention approximately 2/3 of the patients showed the symptoms of a postembolization syndrome. Elevated body temperature could be documented in 31 patients (73.8%). A total of 27 (64.3%) patients had postinterventional pain. In 15 (35.7%) patients nausea or vomiting was reported.

Figure 3 shows survival in months in patients receiving palliative embolization. The median survival time was 13.5 ± 10.8 months, with the shortest survival being 1 month and the maximal one 56 months. Fourteen patients were still ali-

ve. The patients in this group were in the stage M0. In 2 of the patients not included in the study with small tumors (2 cm), angiographic findings were negative, so that embolization could not be performed. These patients underwent thermoablation.

Figure 4 shows CT scan in a patient with a small tumor on the left kidney and negative angiographic findings.

Figure 5 shows renal tumor immediately after embolization and a few days after embolization with air development.

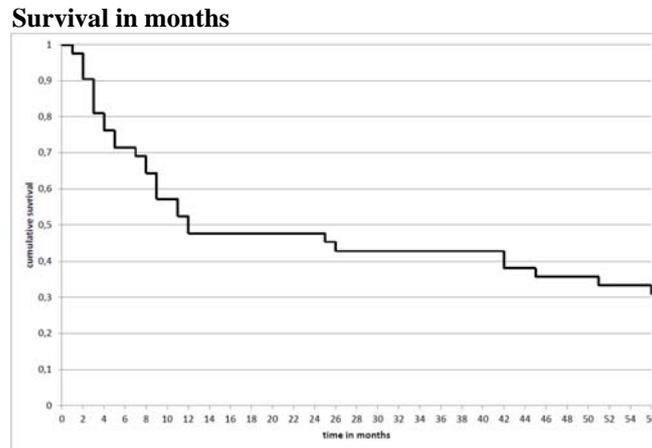


Fig. 3 – The survival time in patients receiving palliative embolization of renal tumors.

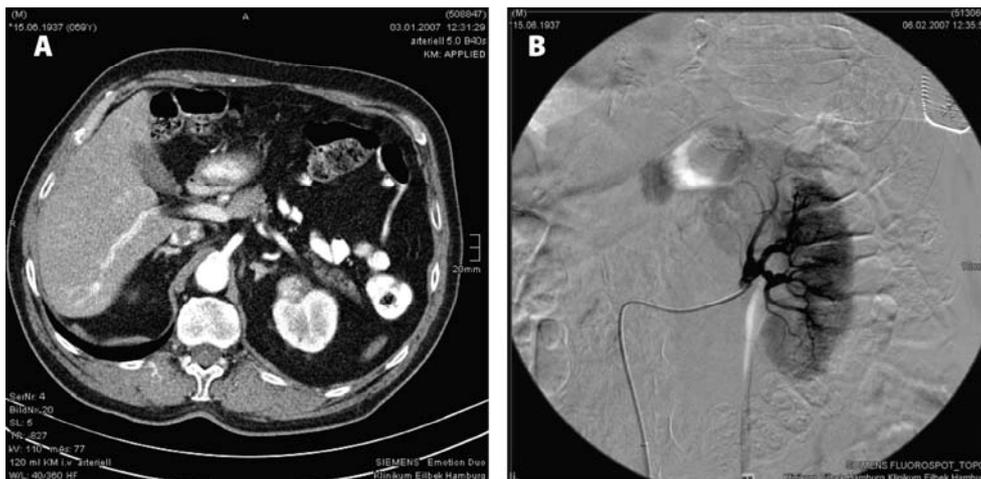


Fig. 4 – a) Computed tomography scan in a patient with small tumor on the left kidney; b) negative angiographic finding in the same patient.

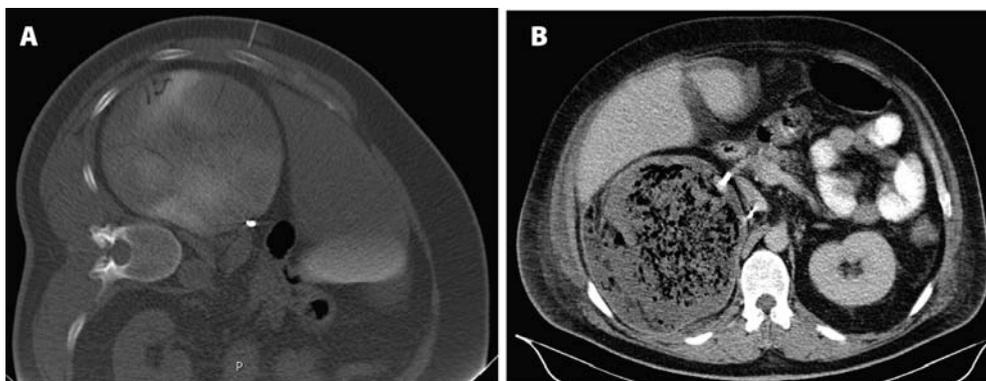


Fig. 5 – Computed tomography scan of renal tumor: a) immediately after embolization; b) a few days after embolization, with the development of air.

Discussion

Palliative embolization is a feasible treatment for patients with inoperable kidney cancer, especially in patients with hematuria or severe pain. These palliative, therapeutic goals are achieved in our patients, which is consistent with the literature^{3,4}.

Capillary embolization in the case of inoperability in asymptomatic patients without distant metastases can induce complete tumor necrosis, showing that embolization is equivalent to nephrectomy. In patients who undertook nephrectomy and were diagnosed with the second tumor on the remaining kidney embolization is one of the therapeutic options. According to our experience patients having a solitary kidney (only one remaining kidney) very often refuse total nephrectomy. It should be noted that in our hospital surgery is the method of choice if enucleation of the tumor is possible. In case of unfavorable location of the tumor, when operational enucleation is impossible, superselective embolization is offered as therapeutic option in which healthy tissue of the remaining kidney is preserved, and patients do not have to undergo hemodialysis.

Advanced inoperable tumors often develop AV shunts which may be disastrous for the patient, as blood flow through these shunts is very large and often leads to right heart failure. Intervention in these patients is not simple and often needs to be repeated at least once. The literature on the survival rate of patients undergoing palliative embolization is controversial. According to Hansmann et al.⁵ in 9 patients that underwent palliative embolization the survival was 3 years in 3 patients with metastases and 6 years and 4 months in 6 patients without metastases.

In the Onishi et al.⁴ study the average survival time of patients in the group that underwent palliative embolization with alcohol was extended to 229 days, compared to the mean survival time of 116 days in the control group without embolization.

Kauffmann et al.⁶ report on the extension of lifespan in 6 patients with metastases by the mean value of 3 years. The embolizations were performed with capillary Ethibloc.

In another study Demirci et al.⁷ report that a group of patients with kidney tumors and metastases that was treated with an adjuvant therapy using interferon-alpha and 5-fluorouracil in combination with nephrectomy, had approximately the same survival rate as a group of patients treated only with embolization.

Hallscheidt et al.⁸ states that in a group of 7 patients with metastases, there was no significant prolongation of life when treated with palliative tumor embolization. In 6 patients without metastases median survival was 2.3 years. The same study reports that other studies have shown the average survival time of 4 to 11 months after palliative embolization.

In their publication from 2007 Maxwell et al.⁹ report the median survival time of 6 months in their group of 19 patients. These authors did not distinguish between patients with or without metastases. This group of patients was very heterogeneous, also including patients with local recurrence after nephrectomy.

Vaicekavicus and Pranculis¹⁰ state that one patient with lung metastases out of the group of 8 patients undergoing palliative embolization lived for 4 years.

Munro et al.¹¹ report in a retrospective study including 25 patients, that restaging was assessed in a period from 27 to 39 months in 14 patients. The results were as follows: in a patients the tumor size increased, in 7 patients the tumor remained unchanged, and in 5 patients there was a decrease of the tumor size.

In patients without metastases there were no cases of newly appearing metastases during the follow-up time. In two patients with metastases a regression of the metastases occurred. All embolizations in this group were performed with absolute alcohol and spirals.

Superselective embolization is performed in cases of small tumors in the remaining kidney (< 4 cm) when surgery is not possible. Additional security for those patients is offered by ablative therapeutic methods such as radiofrequency ablation. We prefer superselective embolization if abnormal blood vessels can be found at angiography. Following embolization, thermoablation is to be performed after 24 hours under CT supervision. In our opinion this approach is a lot more convenient for the patient and for the interventional radiologists. Because renal cell carcinoma is extremely well vascularized tumor, there is a certain risk of bleedings occurring when puncturing the tumor, which must be treated surgically. We exclude this complication by previous embolization. It is interesting to note that in two patients out of our group of patients with small renal tumors the size of 2 cm we did not have positive angiographic findings. In both patients only thermoablation was performed, which passed without complications. One of the above-mentioned two patients had multiple metastases to the spine that were surgically treated, and histopathology confirmed that the metastases originated from a clear-cell renal tumor.

At the beginning of the era of embolization a complication rate of about 4% was described in the literature¹². During the beginnings of embolization a group of authors in Germany applied alcohol without using occlusion catheter, leading to more serious complications. Löhr and Ross¹³ describe death during embolization of tumors of the right kidney with alcohol, probably due to massive pulmonary embolism. In this patient an AV malformation was identified, so the authors assume a direct crossing of alcohol into the venous circulation, which led to pulmonary embolism. Several authors¹⁴⁻¹⁶ report bowel infarction as a complication during embolization. Besides, Laarmann et al.¹⁷ and other authors¹⁸ also report gonadal damage during kidney embolization. Individual descriptions of paraplegia as a result of renal embolization exist in literature^{19,20}.

In recent studies, also, it has been reported that after embolization approximately 75% of the patients develop postembolization syndrome that lasts shortly²¹. The same authors report further complications such as hematoma or dislocation of spirals. The administration of corticosteroids before the intervention can reduce the occurrence of postembolization syndrome²². After embolization of renal tumors air bubbles are frequently seen in embolized tumor in the early postembolization phase. The quantity of air is a valuable me-

asure for the breakdown of tumor. Although at this stage there is leukocytosis and an increase in temperature, there is no abscess. Air bubbles develop from protein destruction with the release of oxygen which can not be dissolved in the region of the coliquation necrosis. At the beginning of the era of embolization the exact cause of air bubbles in embolized tumors was unknown. Bacteria that produces gases was assumed to be responsible for this situation²³. In later works it is stated that the sterile products of tumor cells decomposition are responsible for the development of gas bubbles²⁴.

It is well known from embolizing other organs that abscess formation can occur after embolization. Sometimes it is difficult to discern whether symptoms like temperature and leukocytosis develop due to a postembolization syndrome including sterile gas formation or due to abscess formation. The answer to this question is given by follow-up CT scans proving the considerable colliquation of the abscess close to

air, as well by clinical and laboratory findings showing prolonged fever and an increase of the inflammatory parameters. Mostly large tumors are likely to form abscesses after embolization. Sometimes general condition of patient's is so bad that drainage must be performed after nephrectomy.

With our embolization technique we had no serious complications in terms of reflux and unwanted embolization into other vascular regions including the venous system.

Conclusion

Our results are consistent with data in the literature. Survival in patients without metastases was longer than in those with metastases, as confirmed by 14 of the patients from the study. An additional therapeutic safety in the treatment of small cancers is provided with a combination therapy of embolization and radiofrequency thermoablation.

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