Renal Pseudoaneurysms and Arteriovenous Fistulas as a Complication of Nephron-Sparing Partial Nephrectomy: Technical and Functional Outcomes of Patients Treated With Selective Microcoil Embolization During a Ten-Year Period

Interventionelle Behandlung renaler Pseudoaneurysmen und AV-Fisteln als Komplikation nach partieller Nephrektomie: Technische und funktionelle Ergebnisse von allen mit selektiver Microcoil-Embolisation behandelten Patienten eines 10-Jahres-Zeitraums

Zusammenfassung

Ziel: Das Ziel dieser Studie war das klinische und funktionelle Ergebnis der Patienten zu untersuchen, die mit einer interventionellen, selektiven Embolisation von renalen Pseudoaneurysmen oder AV-Fisteln an unserer Klinik behandelt wurden.


Schlussfolgerung: Eine kathetergesteuerte Embolisation ist eine erfolgversprechende organerhaltende Therapieoption.

Abstract

Purpose: The aim of this study was to evaluate the clinical and functional outcomes in patients who underwent selective interventional embolization of renal pseudoaneurysms or arteriovenous fistulas at our center.

Materials and Methods: Our retrospective analysis included all consecutive patients who received selective transcatheter embolization of renal pseudoaneurysms or arteriovenous fistulas after partial nephrectomy in our department from January, 2003 to September, 2013. The technical and clinical success rate and functional outcome of every procedure was collected and analyzed. Furthermore, the change in renal parenchymal volume before and after embolization was determined in a subgroup.

Results: A total of 1425 patients underwent partial nephrectomy at our hospital. Of these, 39 (2.7 %) were identified with a pseudoaneurysm or an arteriovenous fistula after partial nephrectomy. The diagnosis of the vascular lesions was made by means of biphasic CT or CEUS. Technical success by means of selective microcoil embolization was achieved in all 39 patients (100 %). Clinical success, defined as no need for further operation or nephrectomy during follow-up, was achieved in 35 of 39 patients (85.7 %). Renal function, as measured by eGFR before and after the intervention, did not change significantly. However, a mean loss of parenchymal volume of 25.2 % was observed in a subgroup. No major or minor complications were attributable to the embolization procedure.

Conclusion: Transcatheter embolization is a promising method for treating vascular complications which may occur after partial nephrectomy. We confirm the high success rate of this technique while discussing renal functional outcomes and potential safety aspects.
tende Methode zur Behandlung vaskulärer Komplikationen, die nach partieller Nephrektomie auftreten können. Wir bestätigen die hohe Erfolgsrate dieser Technik und analysieren funktionelle renale Endpunkte sowie Sicherheitsaspekte.

Kernaussagen:
- Arterielle Pseudoaneurysmen oder arteriovenöse Fisteln sind seltene, jedoch schwerwiegende Komplikationen nach partieller Nephrektomie
- Die selektive Mikrocoil Embolisation ist ein sicheres nierenerhaltendes Verfahren zur Behandlung dieser Komplikationen
- Die Embolisation führt zu einem signifikanten Verlust des Nierenparenchymvolumens aber zu keinem renalen Funktionsverlust

Introduction

Partial nephrectomy is a well-established operative procedure for the treatment of renal tumors \cite{1, 2}. This nephron-sparing surgery shows similar oncologic outcomes when compared to total nephrectomy \cite{3–5}. In addition, it is associated with a lower risk of post-operative chronic renal failure \cite{3, 6, 7}. However, partial nephrectomy increases the risk of iatrogenic vascular lesions, such as pseudoaneurysms and arteriovenous fistulas, due to the highly vascularized renal parenchyma \cite{8, 9}. They are rare but serious complications which can lead to severe hematuria, blood loss, and hemorrhagic shock \cite{8, 10}. It has been reported that these arterial lesions can be treated successfully with minimally invasive selective transcatheter embolization \cite{11–14}. However, the published studies on this topic are relatively small, with the largest study to date, to our knowledge, reporting about a cohort of 28 patients \cite{11}. In addition, the effects of embolization on quantitative renal parenchymal volume and procedure-related radiation dose have not been previously reported. Therefore, this study was performed to further define the role of embolization in the management of renal vascular lesions after partial nephrectomy. The purpose of this study was to evaluate all consecutive patients who received transcatheter embolization for the treatment of renal vascular complications after partial nephrectomy at our institution. Technical and clinical successes, radiation doses, and the influence of the embolization on renal function and volume are reported.

Materials and Methods

Patients and technical and functional outcomes
All consecutive patients who underwent angioembolization of iatrogenic vascular lesions due to partial nephrectomy were identified through a search of our database, which includes all radiological interventions performed at our department. Medical charts, laboratory investigations, and radiological reports of all patients were carefully reviewed to determine technical and functional outcomes of the interventions. Glomerular filtration rate (GFR) was determined one day before and one day after partial nephrectomy as well as one day before and one day after angiembolization. GFR was estimated using the Cockcroft-Gault equation with the parameters age, sex, and serum creatinine levels \cite{15}. Technical success was defined as successful primary angiography-guided occlusion of the arterial lesion. Clinical success was defined as no need for nephrectomy or further operation on the vascular lesion during follow-up.

Pre-interventional imaging
In all patients, pre-interventional imaging was performed to localize and confirm the clinically suspected vascular lesion. Patients underwent a biphasic contrast-enhanced CT examination consisting of an arterial and venous phase of the abdomen as the primary imaging modality. In patients with severely reduced GFR, contrast-enhanced ultrasound was performed as an alternative imaging modality. CT examinations were performed on a 64- or 128-row scanner (Siemens Healthcare®, Erlangen, Germany) with the use of 1.5 ml of contrast agent per kg of body weight (Imeron 400®, Bracco Imaging, Konstanz, Germany) followed by a bolus of 100 ml of sodium chloride. Sonographic evaluation consisted of an examination using B-mode, color duplex ultrasound, and contrast-enhanced sonography. Contrast-enhanced sonography was performed after injection of 0.8–1 ml of contrast agent consisting of microbubbles (SonoVue®, Bracco, Milan, Italy) followed by a bolus of 10 ml of NaCl. Ultrasound examinations were carried out either on a LOGIQ E9® (GE Healthcare®, Little Chalfont, United Kingdom) or an S2000® (Siemens Healthcare®, Erlangen, Germany).

Interventions
Through a femoral access, a renal angiogram was first performed to localize the vascular lesion using a 4F catheter (Terumo®, Tokyo, Japan). Afterwards, superselective catheterization of the bleeding vessel was performed using a coaxial microcatheter system (Progreat®, Terumo, Tokyo, Japan). When a stable catheter position was obtained, coil embolization was performed until complete occlusion of the vascular lesion was achieved. The coil type used depended on the preference of the interventionalist. The types and sizes of the coils used will be presented in the results section. All interventions were performed by board-certified interventional radiologists with at least five years of experience in embolization procedures. Volumetric analysis
Axially reconstructed images with 5-mm slice thickness from the pre- and post-interventional CT scans in the portal venous phase were used for volumetric analysis. This was performed using semi-automated volumetric software (Siemens Syngo.via® Oncology, Siemens Healthcare®). A digital dash was drawn across the whole kidney, after which a volumetric segmentation of the kidney was obtained. Manual correction of the contours was...
then performed. The two volumes obtained (pre- and post-intervention) were recorded and the volume shrinkage between pre- and post-intervention was calculated. Volumetric measurements were performed in consensus by two diagnostic radiologists, one with three years and the other with six years of experience in this procedure.

Ethics statement
All investigations have been conducted according to the principles expressed in the Declaration of Helsinki. All patient records and information was anonymized and de-identified prior to analysis. Therefore, and due to the strictly retrospective design of the study, no written informed consent was obtained by the participants. The institutional review board of the ethics committee of Ludwig-Maximilians-University confirmed the study with a certificate of compliance (No. 526–15 UE).

Statistical analysis
Categorical variables are presented as absolute and relative frequencies. For descriptive data with normal distribution, mean ± standard deviation (SD) was given, and comparisons were performed by a 2-sided t test. A p-value <0.05 indicated statistical significance. All analyses were performed using SPSS® software (version 20, IBM SPSS Inc.).

Results

Between January, 2003 and September, 2013, a total of 1425 patients underwent partial nephrectomy at our institution. Of these, 39 (2.7 %) were referred to our department for transcatheter embolization of pseudoaneurysms or arteriovenous fistulas (mean age 65.7 years; 30 males, 9 females). Baseline demographics of the cohort are given in Table 1. In total, we had 26 patients with at least one renal pseudoaneurysm, 12 patients with AV-fistulas, and 1 patient with a pseudoaneurysm and an additional AV-fistula. The patients of this study underwent open, laparoscopic, or robot-assisted surgery; the greatest proportion (82.1 %) was treated with open partial nephrectomy. Patients presented clinical symptoms of the vascular lesion 15.3 days (mean) after partial nephrectomy. Diagnosis was established by biphasic CT in 92.3 % of cases and by CEUS in 7.7 % of cases. Occlusion of the vascular lesion was accomplished with a mean of 4 coils (range 1–26). Tornado coils (Cook, Bjaeverskov, Denmark) with a size range of 3–10 mm were used in 36 patients. An Interlock occlusion system (Boston Scientific, Marlborough, MA, United States) was employed in two patients (Interlock coils with a size of 6×100 mm in one patient and one Interlock coil with a size of 12×200 mm in the other patient). A detachable HydroCoil (Azur®, Terumo, Tokyo, Japan) was used for embolization in one patient. The mean intra-interventional dose area product was 8563 cGy × cm² (range 1287–36701 cGy × cm²). Characteristics of the interventions are shown in Table 2.

Overall, primary coil embolization was technically successful in 39 patients (100 %). However, a second intervention with additional embolization was necessary for two patients in this group (5.1 %). Clinical success, with no need for further operation or nephrectomy, was achieved in 35 patients (89.7 %). Four patients (10.3 %) had to undergo surgery after angiembolization due to persistent blood loss and hematuria. In three of these four patients, persisting clinical symptoms were severe enough that nephrectomy had to be performed, and in one patient an operative revision with suturing of the arterial lesion was performed. Examples for successful interventions and preinterventional imaging are presented in Fig. 1, 2.

No typical complications of invasive angiography, such as dissections, groin hematoma, or bleeding, were observed in any intervention. Although there was a significant reduction of GFR between the pre-operative and post-operative days, there was no significant difference of GFR between the pre-embolization and post-embolization days. Details about the analysis of renal function are given in Table 3.

Determination of renal loss of volume could be determined in a subgroup of n = 10. In the remaining 29 patients, post-interventional renal volume could not be determined because patients were either lost to follow-up or underwent follow-up in a different hospital or private practice or underwent follow-up by MRI. All pre-interventional volume measurements were performed in the CT scan before embolization. Post-interventional volume was measured in the first post-interventional CT scan, which

Table 1 Baseline demographics.

<table>
<thead>
<tr>
<th>characteristics</th>
<th>number (percentage) or mean ± SD (range)</th>
</tr>
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<tbody>
<tr>
<td>total number of patients</td>
<td>39 (100)</td>
</tr>
<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>– male</td>
<td>30 (76.9)</td>
</tr>
<tr>
<td>– female</td>
<td>9 (23.1)</td>
</tr>
<tr>
<td>age, mean ± SD (range) in years</td>
<td>65.7 ± 11.8 (32–81)</td>
</tr>
<tr>
<td>tumor size, mean ± SD (range) in cm</td>
<td>3.8 ± 1.6 (1.2–8.5)</td>
</tr>
<tr>
<td>operative approach</td>
<td></td>
</tr>
<tr>
<td>– open</td>
<td>32 (82.1)</td>
</tr>
<tr>
<td>– laparoscopic</td>
<td>4 (10.3)</td>
</tr>
<tr>
<td>– robot-assisted</td>
<td>3 (7.6)</td>
</tr>
</tbody>
</table>

Table 2 Intervention characteristics.

<table>
<thead>
<tr>
<th>characteristics</th>
<th>number (percentage) or mean ± SD/median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>days from operation to intervention</td>
<td>15.3 ± 9.7 (3–43)</td>
</tr>
<tr>
<td>imaging modality to confirm diagnosis</td>
<td></td>
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<tr>
<td>– biphasic CT</td>
<td>36 (92.3)</td>
</tr>
<tr>
<td>– contrast-enhanced US</td>
<td>3 (7.7)</td>
</tr>
<tr>
<td>number of coils used</td>
<td>4 (1–26)</td>
</tr>
<tr>
<td>dose area product in cGy × cm²</td>
<td>8563 (1287–36701)</td>
</tr>
<tr>
<td>fluoroscopy time in minutes</td>
<td>13 (2.5–31.4)</td>
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</table>

Table 3 Changes in GFR.

<table>
<thead>
<tr>
<th>mean GFR before partial nephrectomy</th>
<th>mean GFR one day after partial nephrectomy</th>
<th>p&lt;0.01</th>
</tr>
</thead>
<tbody>
<tr>
<td>64.75 ml/min</td>
<td>48.82 ml/min</td>
<td></td>
</tr>
<tr>
<td>mean GFR before embolization</td>
<td>mean GFR one day after embolization</td>
<td>p&lt;0.95</td>
</tr>
<tr>
<td>50.88 ml/min</td>
<td>50.96 ml/min</td>
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</table>
was performed 100 days (median) after embolization. Mean renal volume loss was 25.2 ± 14.3 % between the pre- and post-interventional CT scans, which is a significant loss (p < 0.05). Examples of the volumetric measurements are presented in Fig. 3. Details about volume measurements are given in Table 4.

Discussion

Pseudoaneurysms and arteriovenous fistulas are rare post-operative complications of nephron-sparing partial nephrectomy. At our center, we identified 39 of 1425 patients treated with nephron-sparing surgery (2.7 %) as being affected by one of these iatrogenic lesions. This complication rate is consistent with other reports published in the literature [11, 16 - 19]. Since these complications are potentially life-threatening, it is mandatory to achieve a reliable diagnosis when patients present signs and symptoms potentially indicative of pseudoaneurysms and/or arteriovenous fistulas. Unfortunately, these are often unspecific (as in the case of hematuria, flank pain, hypotension, and fever) or delayed in their occurrence. It has been reported that some patients were even asymptomatic and that the pseudoaneurysms or arteriovenous fistulas in these patients were detected incidentally during examinations for follow-up or another condition [17].

Most of our patients (82.1 %) diagnosed with either pseudoaneurysms or arteriovenous fistulas had undergone open partial nephrectomy, while 10.3 % and 7.6 % were treated with laparoscopic and robot-assisted procedures, respectively. This is in contrast to other reports where a slightly higher occurrence is observed when patients received laparoscopic surgery [12, 17]. This discordance could be explained by the lack of large-scale randomized trials and, possibly, the failure to take confounding factors into account. In addition, a selection bias might be present, given the fact that patients with larger tumors with difficult anatomy, such as a central location, and previously operated patients are more likely to undergo open nephrectomy, which might explain the higher rate of patients being treated with open nephrectomy in our cohort. As yet, no clear reason is known why one or the other surgical procedure would predispose a patient to these vascular complications [20].

Several diagnostic approaches were demonstrated as suitable for the assessment of pseudoaneurysms or arteriovenous fistulas following partial nephrectomy. In 92.3 % of our patient group, CT was used for pre-interventional imaging. This technique has the advantage of not only the detection of pseudoaneurysms and arteriovenous fistulas but also the diagnosis of other intra-abdominal pathologies such as hematoma or urinary retention. Moreover, MDCT is a fast and reliable method [16]. However, pseudoaneurysms may be difficult to differentiate from adjacent arteries. Thus, negative CT-examinations cannot definitely exclude pseudoaneurysms and additional investigations may have

Table 4 Changes in renal volume in each patient of n = 10.

<table>
<thead>
<tr>
<th>patient number</th>
<th>renal volume (ml) before embolization</th>
<th>renal volume (ml) after embolization (Median 100 d)</th>
<th>loss of volume (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>137</td>
<td>124</td>
<td>9.5</td>
</tr>
<tr>
<td>2</td>
<td>192</td>
<td>169</td>
<td>12</td>
</tr>
<tr>
<td>3</td>
<td>182</td>
<td>154</td>
<td>15.4</td>
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<td>4</td>
<td>160</td>
<td>135</td>
<td>15.6</td>
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<td>5</td>
<td>143</td>
<td>114</td>
<td>20.3</td>
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<td>6</td>
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<tr>
<td>8</td>
<td>117</td>
<td>80</td>
<td>31.6</td>
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<tr>
<td>9</td>
<td>165</td>
<td>97</td>
<td>41.2</td>
</tr>
<tr>
<td>10</td>
<td>186</td>
<td>85</td>
<td>54.3</td>
</tr>
<tr>
<td>mean loss of volume: 25.2 ± 14.3 % (p &lt; 0.05)</td>
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to be performed [12]. In patients with severely impaired renal function, the use of nephrotoxic contrast media can pose an unacceptably high risk. In these cases, contrast-enhanced ultrasound or MRI without contrast agents are more suitable. For this reason, diagnostic imaging of our patients with a severely lowered eGFR (7.7 %) was performed utilizing contrast-enhanced ultrasound. However, contrast-enhanced ultrasound is highly dependent on the experience and knowledge of the performing physician. Therefore, it may not be readily available in many institutions.

Even if CECT and CEUS are preferred because of their non-invasive nature, percutaneous angiography may be required although it presents a higher morbidity and mortality risk and cannot image the entire urinary tract [18]. When there is a strong suspicion of a pseudoaneurysm or an arteriovenous fistula, angiography with a subsequent embolization procedure may be a straightforward approach [13]. Despite these alternative options, however, CECT is the first choice both for diagnosis and for follow-up unless substantial contraindications exist [18].

In our cohort, symptoms indicating the existence of a vascular lesion and the consecutive positive diagnoses thereof appeared 15.3 days (mean; range 3–43 days) after partial nephrectomy. This time interval corresponds to findings in the literature which show that pseudoaneurysms or arteriovenous fistulas were detected from one day up to several months after surgery, with an approximate mean of between 8 and 15 days [11, 12, 17, 18, 21, 22]. In one small study, the longest interval between operation and clinical symptoms was even 3 months [23]. The largest study on this topic, which was recently published, examined the timing and indications of transcatheter angiographic embolization for delayed hemorrhage after percutaneous nephrolithotomy in 144 patients [24]. Their reported mean time to the onset of post-nephrolithotomy hemorrhage was 10.5 days (range 2–30 days), which is in line with our results after partial nephrectomy. These observations underline the need for alertness when symptoms begin to manifest within the follow-up period.

Selective embolization of the leaking arteries was accomplished by complete occlusion of the feeding arteries using microcoils. According to the interventionalists’ preferences, several types of coils were utilized. In most cases (36 of 39 patients) Tornado® coils were employed (similar to a.o. [13, 18]). Coil embolization proved to be highly effective and allowed for complete closure of the target vessels. However, autologous blood clots, detachable balloons, gelatin sponges, and several liquid embolic agents (such as glue and the non-adhesive Onyx®) have also been shown to perform adequately. The latter impose a higher risk of reopening or are associated with higher costs. In specific anatomical situations as well as in patients with poor coagulation parameters, however, they may be the better choice [13]. Microcoil embolization enables isolation of the vascular lesion while retaining maximal renal vascularization, thus ensuring as much preservation of the renal parenchyma as possible [16].

The intervention was technically successful in 100 % and clinically successful in 89.7 % of our patients. In two patients of our collec-
dures (To our knowledge, we are the first to quantitatively evaluate renal significance was absent, likely because of the small patient sample.

decrease in eGFR values before and after intervention, statistical further as measured by eGFR. These observations are similar to those reported by Gahan et al. [11]. Interestingly, although they experienced interventional radiologists is a safe procedure.

A review of the eGFR values before and immediately after surgery and transcatheter embolization shows that renal function sig-

ificant reduction of functional renal parenchyma. However, this volume loss of renal parenchyma was not associated with a significant reduction of renal function, as proven by eGFR measurements. Only one recently published study has semiquantitatively assessed renal parenchymal volume loss after embolization [26]. They reported a mean volume loss of 5% with a range of 1–50%, which is in line with the range of our study.

Radiation exposure in patients associated with embolization of pseudoaneurysms and arteriovenous fistulas following partial nephrectomy has not been reported previously. The mean dose area product was 8563 cGy × cm², with a wide range of 1287–36 701 cGy × cm². The wide range may be due to the different generations of angiographic equipment used during the ten-

year period of the study as well as the different extent and severity of the vascular lesions treated, which is also reflected in the wide range of coils used (1–26). More effort should be made to reduce the radiation doses of these interventions in the future. The mean fluoroscopy time was 13 minutes, which is an accepta-

bly low exposure time. Nevertheless, a shortening of the latter could reduce the radiation effect since a correlation exists be-

tween the two [27]. Several limitations of this study inherent to its retrospective nature and small sample size have to be taken into account. However, since pseudoaneurysms and arterio-

neous fistulas following partial nephrectomy are rare, our study group is the largest reported to date. The analysis of renal func-

tion was performed by determining the eGFR according to the Cockcroft-Gault formula, which is only an approximate indicator of renal function. Volumetric analysis of the renal parenchyma could only be performed in a small subgroup (n = 10). This was due to the fact that in the remaining 29 patients, post-interven-

tional renal volume could not be determined because patients were either lost to follow-up or underwent follow-up in a differ-

ent hospital or private practice or underwent follow-up by MRI. Moreover, the time interval between embolization and the follow-

up CT was variable. Finally, a long-term follow-up of the kidney function would provide more information.
Conclusion

Transcatheter angioembolization is a promising method for treating pseudoaneurysms and arteriovenous fistulas, which are rare but dangerous vascular complications which may occur after partial nephrectomy. Our results show a high technical success rate and no significant decrease in renal function in the early post-embolization period. We assessed the changes in parenchymal volume and radiation doses to which patients are exposed during intervention. In order to provide a clear answer as to which method of diagnosis and angioembolization treatment is superior with regard to maintaining as much renal function as possible, large-scale prospective studies, including a long-term follow-up of renal function, should be performed.

Clinical Relevance of the Study

- Renal pseudoaneurysms and arteriovenous fistulae can be treated successfully and safely with endovascular embolization.
- Although embolization reduces the renal parenchymal volume, it preserves the organ and its function.
- Arterial lesions, which occur after partial nephrectomy should therefore be treated first with embolization by interventional radiologists.

References

3. Buddharto T, Joniau S, Lerut E et al. Prospective evaluation of 11C-choline positron emission tomography/computed tomography and diffusion-weighted magnetic resonance imaging for the nodal staging of prostate cancer with a high risk of lymph node metastases. European urology 2011; 60; 125 – 130