Urological complications following radiofrequency ablation of renal tumors

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Purpose

• Small renal tumors should benefit from a specific management due to:

  - the increased incidence related to generalization of abdominal imaging (+11% 1993-2004, specifically in 7-9th decade)
  - the increased incidence of chronic renal failure in the elderly population
  - the efficacy of conservative urological treatment

• Percutaneous ablative treatments benefit from strong technological developments (radiofrequency ablation, cryotherapy, micro-wave ablation…). The reference treatment for renal cancer remains surgical resection (using at best nephron sparing surgery)

• Among radiofrequency ablation complications, urinary tract lesions can be severe leading to definitive urine diversion or even nephrectomy. Deeply located tumors are the most exposed to urinary tract injury.

• Pelvic protection can be achieved by cooling down the urinary tract injecting a cold fluid (5% glucose) through a ureteral catheter. The efficacy of this technique has been mostly evaluated in animals by retrograde injection or more recently, by percutaneous nephrostomy. This cooling might reduce the incidence and the size of urinary tract fistula [1-8].

• However, pelvic cooling has multiple drawbacks including:

  - additional invasive procedure
  - general anesthesia required in men (retrograde ureteral stent)
  - technical limitations and difficulties leading to catheterization failure, ureteral perforation, obstruction of the urinary tract by clotting
  - infectious complications (acute prostatitis or pyelonephritis)
  - theoretical decrease of RFA efficacy
  - percutaneous nephrostomy complications (failure, hematoma, arterio-venous fistula, false-aneurysm, haematuria)

• The aim of our study was to evaluate the type, incidence and risk factors of urological complications after RFA of renal tumors
Methods and Materials

• Retrospective study performed for a period of 7 years including 182 consecutive patients:
  - age: 61±17 years (min 18-max 90)
  - sex-ratio: 1.56 (111 men / 71 women)

• A total of 295 tumors were treated, with:
  - 2 procedures for 18 tumors,
  - 3 procedures for 4 tumors,
  - 4 procedures for 2 tumors,
  - 5 procedures for 1 tumor.

• Patient population:
  - 60 patients had hereditary renal tumors (von Hippel Lindau disease (56), Birt-Hogg-Dube syndrome (2), Tuberous Sclerosis (2))
  - Among the 320 procedures, 113 were performed in patients with a unique kidney (35%)
  - The glomerular filtration rate was estimated using the Modification of Diet in Renal Disease (MDRD) formula:
    eGFR< 60 ml/min: 130 procedures (44%) (mild renal failure)
    eGFR< 40 ml/min: 56 procedures (19%) (moderate renal failure)
  - The mean of maximal diameters of the 295 tumors initially treated was 25.0 ± 9.4 mm (min 8.7 - max 58.0 mm)
  - The averaged tumor volume (product of 3 diameters x 0.52) was de 8.5 ± 10.7 ml (min 0.19 - max 75.0 ml)

• Pathology:

  Renal biopsy was systematically performed before or during the procedure except in case of:
  - history of renal cancer, local or contralateral recurrence with similar image findings, occurrence of new lesion or increase in size during follow-up
  - von Hippel Lindau disease with typical imaging features of RCCs, occurrence of a new lesion or increase in size during follow-up
- Birt-Hogg-Dube syndrome and hereditary papillary cancer with typical imaging features (low signal intensity on T2w MRI)

Histologically entities: proven or highly probable RCC: 61%; proven or highly probable papillary cancer 9.1%; chromophobic cancer 3.1%; oncocytoma 1.7%; angiomyolipoma 1.3%; biopsy failure or not done (23.4 %)

• Tumor classification:

Tumors were classified into 5 stages according to their anatomical location:
- stage I: tumor volume out of renal parenchyma: > 75%
- stage II: tumor volume out of renal parenchyma: 50-75%
- stage III: tumor volume out of renal parenchyma: 25-50%
- stage IV: intraparenchymal tumor volume
- stage V: tumor located within the renal sinus

• Urinary tract cooling

- The freezing of urinary tract was performed by retrograde ureteral catheterization using a 7F stent (internal /external drainage) or 2 stents when possible. A bladder catheter was systematically inserted

- At the beginning of the procedure, a cold 3L saline bag with 60 mL of low-osmolality iodinated contrast agent (350 mg Iodine/mL) was connected to the ureteral stent

- The injection was performed at very low rate (droplet by droplet) in order to avoid urinary tract dilatation

- Indication of urinary tract cooling was approved by the multidisciplinary cancer committee in cases of:

  - central tumor (stage V), close to the urinary tract, or in case of chronic renal failure

  - tumor stage IV and V in patients with solitary kidney, with or without urinary tract contact

  - tumor stage I to III, with urinary tract contact, mainly in cases of solitary kidney and/or chronic renal failure

• Imaging protocol
The imaging protocol combined Contrast-Enhanced US (CEUS), Contrast-Enhanced CT (CECT) and MRI (CEMRI), depending on patient age and renal function.

It included:
- Before the procedure: ECUS + CECT ± CEMRI
- at day 1 : ECUS + CECT
- at 6-8 weeks : ECUS + CECT ± CEMRI
- at 6 month : ECUS + CECT/CEMRI
- at 12 month and yearly until 5 years : ECUS + CECT/CEMRI

• Statistical analysis

The statistical analysis consisted in calculation of means, SD, min. et max values for all studied parameters.

Patients were classified into 2 groups, with and without urological complications. A correlation with the following parameters was studied using the Fisher test (p= 0.05):
- sexe
- hereditary disease
- solitary kidney
- number of procedure
- side of RFA
- cooling procedure
- contact with urinary tract
- tumor location (stage)

The Wilcoxon test was used for parameters such as age, maximal diameter and tumor volume.
Images for this section:

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Scout view showing the 2 ureteral stents

CT scans confirmed the appropriate position of the 2 stents. The cooling procedure did not lead to pelvis dilatation

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Results

• 8 urological complications were found in 6 patients:
  - 2 urinary fistulas limited to necrotic tumor area (NTAF)
  - 2 urinary retroperitoneal fistulas (RPF)
  - 1 uro-pleural fistula (UPF)
  - 2 RPFs with subsequent hydronephrosis (HN):
    - 1 uretero-pelvic junction stenosis with hydronephrosis leading to destruction of renal parenchyma
    - 1 pelvic scarring with multiple pelvic metastasis leading to destruction of renal parenchyma

• The power of the statistical analysis was limited by the small number of urological complications (6 patients)

No significant correlation was found between urological complications and:
  - age (p= 0.11),
  - sexe (p= 0.69),
  - tumor side (p=0.42)
  - maximal diameter (p= 0.64),
  - tumor volume (p= 0.75)
  - hereditary cancer (p= 1)
  - unique kidney (p= 0.09)
  - contact with urinary tract (p= 1)
  - cooling procedure (p= 1)
  - tumor localization (stage) (p= 0,34)

BUT all complications were seen in patients without cooling procedure

BUT 5 of 6 complications appeared in stage IV tumors

The only statistically significant correlation was found between urological complications and the number of procedures involving residual/recurrent tumors (p= 0.01)
<table>
<thead>
<tr>
<th>Complication</th>
<th>Delay from RFA</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pat1 NTAF1</td>
<td>20 months</td>
<td>No treatment</td>
</tr>
<tr>
<td>Pat2 RPF1</td>
<td>9 months</td>
<td>No treatment</td>
</tr>
<tr>
<td>Pat3 RPF2</td>
<td>6 weeks</td>
<td>Internal ureteral stent during 6 weeks</td>
</tr>
<tr>
<td>Pat4 UPF</td>
<td>2 days</td>
<td>External ureteral stent</td>
</tr>
<tr>
<td>Pat5 RPF3 + hydrenephrosis (HN)</td>
<td>8 days, 6 weeks</td>
<td>No treatment, regression development of sinusal metastases</td>
</tr>
<tr>
<td>Pat6 RPF4 + junction stenosis + HN</td>
<td>7 days, after 8 months</td>
<td>Internal ureteral stent removed at 2nd mouth due to poor tolerance, Treatment refused</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Patients with urological complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td>Pat1 NTAF</td>
</tr>
<tr>
<td>Pat2 RPF1</td>
</tr>
<tr>
<td>Pat3 RPF2</td>
</tr>
<tr>
<td>Pat4 UPF</td>
</tr>
<tr>
<td>Pat5 RPF3+HN</td>
</tr>
<tr>
<td>Pat6 RPF4+HN</td>
</tr>
</tbody>
</table>

Fig. 0

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### Procedure characteristics (overall population; number (%))

<table>
<thead>
<tr>
<th>Localization</th>
<th>Tumors</th>
<th>Urinary tract contact</th>
<th>Stent</th>
<th>Mean Diam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>42 (14)</td>
<td>7 (17)</td>
<td>0 (0)</td>
<td>27.3</td>
</tr>
<tr>
<td>Stage II</td>
<td>45 (15)</td>
<td>10 (22)</td>
<td>2 (4)</td>
<td>23.7</td>
</tr>
<tr>
<td>Stage III</td>
<td>72 (24)</td>
<td>35 (49)</td>
<td>4 (6)</td>
<td>26.4</td>
</tr>
<tr>
<td>Stage IV</td>
<td>128 (43)</td>
<td>68 (53)</td>
<td>13 (10)</td>
<td>22.4</td>
</tr>
<tr>
<td>Stage V</td>
<td>33 (11)</td>
<td>32 (97)</td>
<td>17 (52)</td>
<td>18.9</td>
</tr>
</tbody>
</table>

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**Pat3: Retroperitoneal fistula**

37 year-old woman, von Hippel Lindau, bilateral tumorectomies and repeated RFA sessions for multiple RCC. New central tumor located at the upper pole of right kidney.

- After 1st RFA procedure, persisting enhancing tumor tissue
- Six weeks after 2nd RFA, development of a retroperitoneal fistula
- At 2 months and after internal ureteral stenting, disappearance of the fistula

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Pat4: Uro-pleural fistula (1)

35 year-old woman, von Hippel Lindau disease, bilateral tumorectomy after iterative RFA procedures. Multiple solid tumors of the left kidney.

After 1st RFA procedure: difficult evaluation of the efficacy, tumor recurrence confirmed 1 year after the 1st RFA procedure

Two days after 2nd RFA procedure: left lumbar pain and dyspnea =>

CT revealed the fistula between a renal calyx at the upper pole and the pleura

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**Pat4: Uro-pleural Fistula (2)**

The initial drainage failed due to malposition of the stent (below the UP junction).
At day 16, a new internal/external ureteral catheter was correctly inserted.
At 2 months, CT confirmed the complete disappearance of the fistula and the pleural effusion.

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Pat5: Retroperitoneal fistula with retracted sclerosis of the pelvis and multiple sinusal recurrent metastases (3)
At 3.5 and 4 years after RFA procedure, progression of renal metastases and development of additional tumor sites (liver)

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Pat6: Retroperitoneal fistula and uretero-pelvic junction stenosis (1)

35 year-old man, hereditary papillary cancer, multiple tumors treated by surgery and RFA procedures;
Development of a novel renal tumor at lower pole
At day 0: correct position of the cluster electrode
      (Radionics-Covidien, Cool-tip RF; 15-25)
At day 1: large fat necrosis area surrounding the tumor and reaching the uretero-pelvic junction
Pat6: Retroperitoneal fistula and uretero-pelvic junction stenosis (3)

At 6 months after RFA, persistence of a moderate urinary tract dilatation
The patient refused the placement of a new stent due to the poor tolerance of the previous one
At 2 years after RFA, hydronephrosis resulted in renal destruction

Fig. 0

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Conclusion

• Severe urological complications after renal tumor ablation RFA are rare (0.6 % in our study)

• The treatment of urinary fistulas by ureteral stenting is efficient:
  - internal ureteral stents (pigtailed) for moderate fistula
  - external ureteral stents for severe fistula

• The only statistically significant correlation was found with the number of procedures in cases of retreatment

• The 2 severe complications leading to the loss of kidney function involved:
  - hypovascular tumors
  - with insufficient urine drainage of the fistula

• The cooling procedure with placement of the ureteral stent resulted in additional complications:
  - 1 acute renal failure with obstructive acute pyelonephritis in a patient with solitary kidney,
  - 3 cases of pyelonephritis/acute prostatitis)

• Based on our data, the cooling procedure can be performed in patients with:
  - a unique functional kidney
  - a moderate or severe chronic renal insufficiency

• However, the most critical points in order to prevent urological complications are:
  - the appropriate determination of the needle track,
  - the precision of the electrode guiding,
  - the appropriate choice of the electrode to match the ablated tissue volume to the tumor volume
  - and the optimal placement of the electrodes within the tumor volume without capsular effraction


