Preservation surgery in patients with localized renal cell cancer-Nephron Sparing Surgery

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INTRODUCTION

Renal Cell Cancer (RCC) is third most frequent urological cancer behind Prostate cancer and Bladder cancer. It represents 2-3% of all cancers with annual increase in incidence of 2% in Europe (except Denmark and Sweden) and worldwide. Surgery is the only curative procedure, performed as radical nephrectomy (RN) or partial nephrectomy (nephron sparing surgery –NSS). Radical nephrectomy consists of nephrectomy with ipsilateraladrenalecctomy and lymphadenectomy, but partial nephrectomy means resection of the tumor only with 1-3 mm of healthy surrounding tissue and preservation of the rest of the kidney as well as ipsilateral adrenal gland and lymph nodes. NSS is a method of conservation of attacked kidney and preservation of kidney’s function with previous radical resection of localized RCC, respecting of all oncological principles. The aim of this study is to describe NSS procedure in details and present results of its 13 year use at Clinic of Urology in Novi Sad.

Material and methods: In the last 13 years there were 868 patients(pts) with RCC. NSS has been performed in 242 pts (27,88%). Bilateral tumors: synchronous 8pts,asynchronous 3pts. Better kidney has been operated,first. Indications for NSS were: absolute - 34 pts (15,0%), relative - 58 pts (23,1%) and elective - 150 pts (61,9%).Surgery was performed according to established protocol for this procedure based on recommendation of Prof. A. Novick, Cleveland, USA.

Results: All patients underwent surgery under general anesthesia through lumbotomy, mostly. Tumor size was between 2,5-4,5 cm: over 4,5 cm (47 cm): 4 pts. Average age of pts - 63,5 years (37-84),male: 148 (61,1%), female: 94(38,9%). From 2001-2005, 2006-2010 i 2011-2013, 39,111 i 92 NSS has been done, respectively. It represented 13,5%, 36,6%, 50,54% of all pts with RCC underwent surgery in that period, respectively. There was an increase of NSS in that period compared to RN for localized RCC. There were no death outcomes inpts underwent NSS, local recurrence was seen in 1 patient (0,6%), urine leakage > 2 weeks 5 pts (5/242 =2,06%), severe hemorrhage: 3 pts (1,23%), nephrectomy has been done. We do not have patients with von Hippel Landau (VHL) disease.

Conclusion: Nephron sparing surgery Is the first choice of surgery for patients with low grade kidney tumors (up to 4.5 cm, even 7 cm), has excellent oncological results-comparable with radical nephrectomy, but with preservation of renal function and should be done by an experienced urological team in specialized urological centers with good anesteziological support.

Key words: renal cancer, localized renal cell cancer, nephron sparing surgery
The paraneoplastic syndrome, which is very often seen in patient with RCC, consists of: weight loss, cachexia, anemia, pyrexia, elevated SE rate, hypertension, abnormal liver function, hypercalcemia, polycythemia, amyloidosis.

The only curative treatment for RCC is surgery. Chemotherapy as monotherapy is not considered effective in pts with metastatic RCC and radiotherapy has only pain relief effect in pts with non-resectable brain or osseous metastases.

For metastatic RCC (mRCC) Immunotherapy with Interferon-alpha provide modest response rate of 6-15% and survival benefit of 3-5 months compared to placebo.

Interleukin-2 can be used for mRCC too, with response rate of 7-27% and severe side effects. Monotherapy with Interferon alpha or high-dose bolus IL-2 should not routinely be recommended as first line therapy in mRCC by EAU guidelines.

Today, advances in molecular biology have led to development of several new targeting drugs (target VEGF (vascular endothelial growth factor), receptor kinase and mammalian target of rapamycin: Tyrosine Kinase Inhibitor or mTOR inhibitors) which are approved for treatment of mRCC in USA and Europe(sorafenib, sunitinib, bavacizumab, pazopanib, temsirolimus, everolimus, axitinib).

Cryoablation or radiofrequency ablation of small renal mass, as minimally invasive techniques, are not recommended by EAU guidelines due to low quality of available data. They can be offered only for elderly or co-morbid people with small renal masses, located not in the hilum, proximal ureter or central collecting system and patients with limited life expectancy.

SURGERY FOR RCC

Surgery is the only curative procedure, performed as radical nephrectomy or partial nephrectomy (nephon sparing surgery-NSS). Today, surgery can be done as open, laparoscopic or robotic procedure.

Radical nephrectomy consists of nephrectomy with ipsilateral adrenalectomy and lymphadenectomy, but partial nephrectomy means resection of the tumor only with 1-3 mm of healthy surrounding tissue and preservation of the rest of the kidney as well as ipsilateral adrenal gland and lymph nodes.

There are several types of procedures for preservation of the kidney which is attacked by RCC
- Open/laparo/robotic partial nephrectomy
- Enucleation-tumorectomy
- Partial nephrectomy on the bench and auto transplantation
- Cryoablation
- Radiofrequency ablation (RFA).

NSS is a method of conservation of attacked kidney and preservation of kidney’s function with previous radical resection of localized RCC, respecting of all oncological principles.

Indications for NSS are absolute, relative and elective.

**Absolute:** patient with anatomical/functional solitary kidney (unilateral agenesis, previously performed contralateral nephrectomy, irreversible impairment of renal function of contralateral kidney due to benign diseases), bilateral RCC.

**Relative:** When contralateral kidney has some diseases which could impair renal function, severely: calculosis, chronic pyelonephritis, stenosis of renal artery, vesico-ureteral reflux (VUR) with complications; chronic renal obstructive disease: congenital/acquired; systemic diseases: diabetes, hypertension, nephroangiosclerosis.

**Elective:** patients with small, localized (incidentally detected) RCC and normal contralateral kidney.

Benefit of this conservative procedures should be estimated concerning the age of patient, co-morbidities and risk of progression, which can also compromise rest of renal function.

Several studies have shown that patients underwent NSS have almost the same overall survival (OS), Cancer Specific Survival(CSS), Recurrence-Free Survival rates (RFS) which is comparable with RN for low grade, low stage tumors <4 cm, regardless of the operation approach (open, laparoscopic or robotic).
- In stage T1b (tumor 4-7 cm), T2a(Tu>7cm,<10cm), or T2b (Tu<10 cm, but limited to the kidney), NSS can be done, but there is a lack of conclusive data.
- By one group of authors, open NSS is the best procedure for T1a/b RCC.
TABLE 3
DISTRIBUTION OF RN/NSS PER YEAR

<table>
<thead>
<tr>
<th>Year</th>
<th>RN</th>
<th>NSs</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>71</td>
<td>29</td>
</tr>
<tr>
<td>2012</td>
<td>58</td>
<td>36</td>
</tr>
<tr>
<td>2013</td>
<td>53</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>182</td>
<td>92</td>
</tr>
</tbody>
</table>

TABLE 4
NUMBER OF NSS FROM 2001-2013

<table>
<thead>
<tr>
<th>Year</th>
<th>RCC</th>
<th>NSS</th>
<th>NSS(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>868</td>
<td>242</td>
<td>27.88%</td>
</tr>
<tr>
<td>2013</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- By another group of authors, who are familiar with laparoscopy, laparoscopy is the right procedure for T1a/b RCC.
- With laparoscopy, Warm ischemia time (WIT) is a little longer, complication rate is a little bit higher but oncologic outcomes are comparable and very similar with open procedure. Better cosmetic effect, less bleeding, short hospitalization and faster recovery period are advantages of laparoscopy.

By third group of authors robotic NSS is treatment of choice for T1a/b RCC [14,15,16]. However, authors agree that procedure is technically demanding, has its own steps (which are almost the same for open/laparo/robotic surgery), which should be respected, and should be performed in experienced centers – tertiary institutions (excellent surgical team) [17].

The main goal of surgery is the complete resection of tumor, preservation of renal parenchyma and kidney function and excellent hemostasis.

We are able to do that with resection of 1-3 mm of healthy parenchyma with biopsy “ex tempore” (if necessary), with use of Ultrasound intra-operatively for maximal preservation of renal parenchyma, using wide spectrum of instruments and glues for hemostasis: suture, hemostatic agents, glue, argon beam, surgical bolster, hem o-lock clips.

SURGICAL PROCEDURE

Approach: Extra-peritoneal or trans-peritoneal depends on surgeon’s preference and position of the tumor: posterior tumors -retroperitoneal approach, but anterior, antero-lateral or lateral or a large upper/lower pole tumor require trans-peritoneal approach.

The procedure has several steps:
- Lumbotomy or trans-abdominal approach

Mobilization of the kidney, hilar dissection, hilar clamping-renal vessel control (art/or an block with vein, WIT up to 25 min), excision of the tumor by knife or scissors, oversewing of any large transected intrarenal blood vessels, suturing of collecting system, argon beam coagulation, glue and surgical bolster in bed of the partial nephrectomy defect, parenchymal renorraphy over the bolster, tightening with Weck clip (hem-o-lock clip). Sometimes we can put Z suture on renal capsule to coat the edges of the parenchymal defect. In case of severe bleeding, U shape parenchymal stitches must be put in.

The most common complications of nephron sparing surgery are:
- Urinary fistulas (2.1-17.4%), Infection or abscess (0.6-6%), Bleeding (0-7.9%), Local recurrence (1.4-10%) [18,19].

OUR RESULTS

In the last 13 years there were 868 pts with RCC and NSS has been performed in 242 pts = 27.88%

Bilateral tumors: synchronous 8pts, asynchronous 3 pts. Better kidney has been operated, first.

In the last three years laparoscopic NSS has been done: 1+2+2 = 5pts

Indications for NSS were: Absolute - 34 pts (15.0%), Relative - 58 pts (23.1%) and Elective - 150 pts (61.9%)

Tumor size - 2.5-4.5 cm: over 4 cm (4-7 cm): 4 pts, cystic tumor

Age - 63.5 years (37-84), Male: 148 (61.1%), Female: 94 (38.9%)

Approach
- Extraperitoneal-lumbotomy or trans-abdominal

Our surgical procedure and hemostasis for NSS consist of:

1. Lumbothomy or trans-abdominal approach
2. Mobilization of the kidney
3. Hilar dissection
4. Hilar clamping-renal vessel control (art/or an block with vein)
5. Excision of the tumor by knife or scissors + sometimes we use water jet for dissection
6. Over sewing of any large transected intrarenal blood vessels
7. Suturing of collecting system
8. Argon beam coagulation
9. We do not use glue, but we put a surgical bolster in bed of the partial nephrectomy defect
10. Parenchymal renorraphy over the bolster, we do not use hem-o-lock clip for tightening
11. Sometimes we can put Z suture on renal capsule to coat the edges of the parenchymal defect.
12. In case of severe bleeding, U shape parenchymal stitches must be put in.

Everything (from -12 ) should be done for 25 min.
- We do not have any glue.
- We do not perform lymphadenectomy during NSS. In suspicious cases, frozen section of enlarged lymph nodes is done. If lymph node is positive, radical nephrectomy will be done.
- We also send tumor with surrounding tissue (fat) on PH examination
Time for NSS is between 2-4 h (average: 2.8h), and depends on surgeon and case.

Our complications

Death: 0 %, Local recurrence - 1 patient (0.6%), Urine leakage > 2 weeks 5 pts (5/242 =2.06%)
Severe hemorrhage: 3 pts (1.23%), nephrectomy has been done. We do not have patients with von Hippel Landau (VHL) disease.

CONCLUSION

Nephron sparing surgery:
• Is first choice of surgery for patients with low grade kidney tumors (up to 4.5 cm, even 7 cm)
• Has an excellent oncological results-comparable with radical nephrectomy, but with preservation of renal function
• Should be done by an experienced urological team in specialized urological centers with good anesthesiological support

SUMMARY

POŠTEDNE OPERACIJE KOD LOKALIZOVANOG CARCINOMA BUBREGA-NEPHRON SPARING SURGERY

Uvod: Karcinomi bubrežnog parenhima (RCC) su treći najčešći urološki malignomi iza karcinoma prostate i karcinoma mokraće bešike. Hirurgija je jedina kurativna procedura za lečenje RCC i sprovodi se kroz radikalnu nefrektomiju ili parcijalnu nefrektomiju (nephron sparing surgery-NSS). Radikalna nefrektomija podrazumeva odstranjivanje bubrega sa masnom kapsulom i Gerotinom fascioc, odstranjivanje ipsilateralne suprarenalne žljede kao i pripadajuću limfadenektomiju. Parcijalna nefrektomija podrazumeva resekciju tumora sa 1-3 mm zdravog okolnog bubrežnog tkiva i očuvanje preostalog dela bubrežnog parenhima uz prezervecijsi ipsilateralne nadbubrežne žljede i limfnih žljeda. NSS je metoda konzerviranja obolelog bubrega i očuvanje bubrežne funkcije sa prethodno radikalnom resekcijom lokalizovanog RCC-a, poštujući sve onkološkeprincipes. Cilj ovog rada je da se objasni NSS, predstave indikacije za ovu operaciju kao i način izvodjenja procedure. Na kraju autori prezentuju rezultate NSS u poslednjih 13 godina na Uroškoj klinici u Novom Sadu.

Materijal i metoda rada. U poslednjih 13 godina 868 bolesnika sa tumorima bubrega je operisano na Uroškoj klinici u Novom Sadu, KCV. NSS je urađena u 242 bolesnika (27,88%). Od toga je bilo 8 bolesnika sa sinhronim bilateralnim tumornima, a 3 sa asinhronim. Prvo se uvek operisao bolji bubreg. Indikacije za NSS kod naših bolesnika su bile: Apsolutne u 34 (15,0%), Relativne u 58(23,1%) i Elektivne u 150(61,9%) bolesnika. Operacija je radjena prema etabliranom protokolu za izvodjenje ove procedure baziranom na preporukama prof. Novica iz Clevlenda,USA.

Rezultati rada. Svi bolesnici su operisani u opštoj anesteziji, uglavnom lumbotomijom. Veličina tumora je bilo izmedju 2,5-4,5 cm, dok su tumor preko 4,5cm -7cm imala 4 bolesnika (pretezno cistični tumori). Uzраст bolesnika je bio izmedju 37-84 godine-prosečno 63,5%. Zastupljenost muškaraca je bila 148(61,1%), a žena 94 (38,9%). U periodu od 2001-2005, 2006-2010 i 2011-2013 uradili smo 39,111 i 92 NSS, što je predstavljalo 13,5%, 36,6% i 50,54% u odnosu na sve operacije za RCC u tom periodu. To pokazuje porast primene NSS u odnosu na RN u bolesnika sa lokalizovanim RCC. Nije bilo smrtog ishoda za vreme, niti neposredno posle operacije: 0%. Lokalni recidiv je vidjen u 1 bolesnika (0,6%), Curenje urina >od dve nedelje u 5 bolesnika (2/242 =2,06%) - sanirano plasiranjem ureteralne sonde.

FIGURE 1 SURGICAL PROCEDURE FOR LOCALIZED RENAL CANCER
Značajno kravljene u 3 bolesnika (1,23%) kada je urađena nefrektomija. Nismo imali bolesnika sa Von Hippel Lindou (VHL) bolešću.

Zaključak. NSS je prvi izbor u lečenju bolesnika sa lokalizovanim RCC niskog stepena maligniteta. Ova procedura ima odlične onkološke rezultate koji su komparabilni sa rezultatima radikalne nefrektomije, ali sa NSS se prezervira bubržna funkcija. NSS treba da radi iskusi urološki tim u specijalizovanim urološkim centrima, višeg nivoa sa odličnom anestziološkom podrškom.

Ključne reči: karcinom bubrega, lokalizovani karcinom bubrega, nephron sparing surgery

REFERENCES