

*Aktuelne teme/
Current topics*

PARTIAL AND RADICAL NEPHRECTOMY
IN PATIENTS WITH RENAL CELL
CARCINOMA

PARCIJALNA I RADIKALNA
NEFREKTOMIJA U BOLESNIKA SA
KARCINOMOM BUBREGA

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Abstract

Renal cell carcinoma is one of the more frequently represented malignancies. It is the third most frequent urological cancer with participation of 2-3% of all adult malignancies. In addition to hereditary diseases its appearance is often associated with smoking. Lately clinical presentation is of little importance for its diagnosis which is usually accidental during routine ultrasound examinations. The major role in confirming the diagnosis, making treatment decisions or the type of surgical techniques has the multi slice CT scan. In advanced renal carcinomas the patient prognosis without treatment is poor. Considering treatment modalities, surgery is the most effective method of treatment. Depending on the size and location of the tumor, partial or radical nephrectomy is performed. For decades, radical nephrectomy presented the standard surgical treatment option for treatment of localized renal carcinoma. However in the last decade for treatment of localized renal cell carcinoma, partial nephrectomy is more practiced, as well as laparoscopic and minimal invasive surgical techniques which offer the same oncological results as radical nephrectomy but with decreased morbidity. Approximately 20-30% of patients present with metastasis at the time the diagnosis of renal carcinoma is first made. In the remaining two thirds, 20-30 % develop metastasis after surgical treatment. Metastasis are the main cause of death in these patients. Of all diagnosed patients with renal carcinoma 30-40% die of this illness.

FREQUENCY AND MORTALITY

Renal cell carcinoma (RCC) is the third most frequent urological cancer with participation of 2-3% of all adult malignancies (1,2). Worldwide 270 000 new cases are diagnosed and around 116 000 patients die every year from RCC (3). The incidence of RCC correlates with age with the highest incidence in the sixth and seventh decade. Approximately 80% of patients are between 40 and 69 years of age. Mortality rates in RCC are in constant decrease in the last 10 years. In the period 1990-1994 4.8 /100 000 patients died, but in the period 2000-2004 4, 1 patients/100 000 died of RCC (4,5). The explanation for this decrease in mortality rates probably lies in the early and more frequent incidental diagnosis of small RCC. Thus the overall five year survival rate increases. RCC is more common in males, with the male - to - female ratio of 2:1 (5,6).

Aetiology and pathogenesis

Smoking is a major risk factor for development of RCC. The risk for developing this tumor is increased for 54% in male and 22% in female smokers. There is also a proven direct dose-risk relationship for development of RCC in smokers. Numerous studies have shown an increased risk for RCC in obese patients and in special dietary habits (6-8).

There are a few hereditary illnesses as von Hippel-Lindau (VHL), hereditary papillary RCC, hereditary leiomyomatosis and RCC, Birt-Hogg-Dube syndrome, Tuberous sclerosis, translocation of chromosome 3, associated with RCC and with identified genetic and epigenetic mutations (9).

Different histological types have different prognosis. The most common, and also the most aggressive type is clear cell RCC. It appears in 70-80% of all RCC with the

highest rate of local invasion, metastasis and mortality. Papillary RCC is the second most frequent (15%), followed by chromophobe (5%) and carcinoma of the collecting ducts (1%) (10-12).

More than 30% of patients have metastatic disease at the time the diagnosis of renal carcinoma is first made, and 30% of patients with localized renal carcinoma develop metastasis after surgical treatment (13).

Diagnosis

Many of the patients with RCC are asymptomatic and classic triad of pain, hematuria and flank mass is very rare. So that in more than 50% of patients with renal tumors the diagnosis is accidental during radiological examinations of the abdomen for various diagnostic reasons. The most commonly used diagnostic methods are ultrasound and computed tomography (14-17).

Treatment

Surgical resection is the standard option for treatment of localized renal carcinoma. For decades *radical nephrectomy* (RN) presented the first choice of surgical treatment option of localized renal carcinoma. RN generally implies the excision of Gerota's fascia and its contents (kidney, fat tissue and adrenal gland) and includes extensive lymphadenectomy from the diaphragm to the bifurcation of the aorta (18,19).

However in the last decade for treatment of localized renal cell carcinoma (RCC), partial nephrectomy (PN) is more often practiced, including laparoscopy, due to its minimal invasive surgical techniques offering the same oncological results as RN but with decreased morbidity (20).

Partial nephrectomy (PN) implies the excision of the tumor with a part of surrounding normal renal parenchyma. Initially PN was performed in absolute indications, i.e. in anatomical and functional solitary kidneys. Relative indications are renal tumors in patients who have co morbidities that can compromise present and future renal function (diabetes, hypertension, calculosis, chronic pyelonephritis and renal artery stenosis of the contra lateral kidney). Because of good oncological outcomes and results following PN in absolute indications, as well as in widespread use of ultrasound and accidental detection of low stage and grade tumors, indications for PN are rapidly expanded and include patients with a normal contra lateral kidney (21-24).

PN nephrectomy has overtaken the lead in the treatment of renal tumors up to 4 cm (T1a stage), in selected patients with tumors from 4-7 cm (stage T1b) and is equally reliable as RN. So far there isn't a adopted unique and definite approach considering the role of PN in treatment of tumors 4-7 cm when there are no absolute indications for this type of surgery. The majority of referent studies provide data that from the oncological point of view considering „cancer free survival” PN is equally reliable as RN (25-31).

Partial nephrectomy can preserve more renal function and reduce the risk of development of chronic kidney disease compared with RN. Excellent cancer control and a low local recurrence rate can still be achieved with PN for T1 tumours (32).

Processing 6042 patients with renal tumors during 2012 in Great Britain, 1768 where stage T1, respectively with tumors up to 7 cm. Of this number in stage T1a 55, 6%

patients were treated by PN whereas 18.9% of patients in stage T1b were treated by conservative surgery. Results obtained showed that conservative surgery was mostly used in small tumors up to 4cm, whereas in tumors from 4-7cm in more than 80 % of cases RN was the method of choice (33). This study shows the reality and preference of the surgeon to RN in larger tumors, either due to their localization or fear of possible complications or local recurrence.

Van Poppel et al. in the EORTC study in over 500 patients with renal tumors stage T1a and T1b up to 5cm and normal contra lateral kidney showed that both methods have outstanding oncological results. Respectively PN from the oncological point of view is as effective as RN. They also note that the trend favored RN for treating larger tumors is now obsolete (34).

Also, if one takes out as criteria quality of life, renal function and overall survival, most authors agree that PN has an significant advantage over RN (35-37).

Locally advanced tumors invade renal veins, vena cava, peripelvic and perirenal fat tissue, adrenal gland or extending out of the Gerota fascia (38).

There is no doubt that treatment of choice for locally advanced RCC is surgery because of significantly increased cancer-specific survival (39). Despite RN, there is a significant risk of recurrence and progression compared to localized RCC. The overall ten- year survival rate for these patients is about 12-36% (40).

Approximately 40-50% of patients present or develop metastasis. Untreated patients with disseminated disease have an average survival time less than 12 months, with a five- year survival of less than 10%. (41) If metastasis are confined to one organ or can be surgically removed ,surgical resection is the standard treatment option (42). The discovery of specific genetic alterations has lead to development of new drugs that block some of the paths responsible for progression of RCC, primarily vascular endothelial growth factor or mammalian target of rapamycin. In such patients, the average specific tumor survival of several years can be doubled. However, the treatment with these novel drugs is still palliative and very expensive (43,44).

CONCLUSION

Renal cell carcinoma participates to 2-3% of all adult malignancies. It is usually asymptomatic and often accidentally discovered during radiological procedures for other reasons. For diagnosis, to determine the extent of the disease as well as the optimal treatment, multi-slice CT scan has a significant role. Surgical resection is a standard treatment option. Sparing surgery in the last decade takes precedence in treating patients with tumors up to 4 cm and in selected patients with tumors 4-7 cm and larger. Metastasis is the main cause of death in patients with RCC. They are present in one third of patients at the time of diagnosis, and in 20-30% of the others develop postoperatively. Survival depends on the severity of the illness at the time of diagnosis and of co morbidities. Unlike the patients with localized tumor whose prognosis is good, treatment of patients with invasive and metastatic disease is still inadequate. The prognosis of these patients is poor with a small survival rate.

Sažetak

Karcinom bubrega spada u češće zastupljene malignitete. On je je treći najčešći urološki kancer. Sa učešćem od 2-3% svih malignih tumora kod odraslih, zauzima trinaesto mesto. Pored hereditarnih oboljenja, njegova pojava se često vezuje za pušenje. U poslednje vreme klinička slika je od malog značaja za njegovo otkrivanje. Dijagnoza se postavlja najčešće slučajno i to pri rutinskim ultrazvučnim pregledima. Za potvrđivanje dijagnoze i donošenju odluke o načinu lečenja, odnosno o vrsti operativne tehnike značajnu ulogu ima multislajnsni skener. Kod uznapredovalih slučajeva, prognoza bolesnika bez terapije je infaustna. U terapijskom pogledu, metoda izbora je hirurški zahvat. U zavisnosti od veličine i lokalizacije tumora, vrše se poštedne (parcijalne) ili totalne (radikalne) nefrektomije. Decenijama unazad radikalna nefrektomija je predstavljala operaciju izbora za lečenje organ-ograničenog karcinoma bubrega. Međutim, u poslednjoj deceniji u lečenju lokalizovanog karcinoma bubrežnih ćelija najčešće se koristi parcijalna nefrektomija, kao i laparoskopije i minimalno invazivne hirurške tehnike koje nude iste onkološke rezultate kao i radikalna nefrektomija, ali uz manji morbiditet. Najčešća komplikacija oboljenja su metastaze. One se verifikuju kod 20-30% bolesnika na prvom pregledu, a kod ostale dve trećine takođe 20-30 % bolesnika razvije metastaze nakon operativnog lečenja. Metastaze su i glavni uzrok smrtnog ishoda. Od svih dijagnostikovanih bolesnika sa karcinom bubrega oko 30-40% umire od ove bolesti.

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