# 3D laparoscopic enucleation vs standard partial nephrectomy for cT1 renal masses: assessment of functional outcomes at 1-year follow-up

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**3D laparoscopic enucleation vs standard partial nephrectomy for cT1 renal masses: assessment of functional outcomes at 1-year follow-up**

AIM: *To evaluate renal function after laparoscopic nephron-sparing surgery (NSS) and to establish the factors that might influence its dynamic one year after surgery.*
METHODS: *The prospective study included 83 patients previously diagnosed with renal cell carcinoma who underwent laparoscopic NSS. Demographic, clinical, laboratory and surgery related data were recorded. Patients were followed up for one year after surgery.*
RESULTS: *The majority of cases (63 (76.8%)) were included in stage T1a. Almost two thirds of patients underwent partial nephrectomy (PN) (54 (65.1%)). A slight decrease in GFR was observed 1 year after surgery (80.1±21.5 ml/min; 75.3±22.4 ml/min respectively) in all patients. Univariate analysis showed a significant decrease in GFR values one year after surgery for patients who underwent standard PN as compared with those from the enucleation group (p=0.003). Male patients showed a significant decrease in GFR one year after surgery, as compared with female patients (p<0.001), and elderly patients were more likely to show lower GFR. When considering the simultaneous influence of age, gender and type of surgery on the evolution of GFR, the threshold for statistical significance was slightly crossed (p=0.2).*
CONCLUSION: *Partial nephrectomy as compared to enucleation, advanced age and male gender are associated with impaired renal function at one year after laparoscopic NSS.*

KEY WORDS: Enucleation, Laparoscopic partial nephrectomy, Renal cell carcinoma

## Introduction

Renal cell carcinoma (RCC) is the most common type of kidney cancer in adults. In the United States, RCC represents approximately 3% of all adult malignancies and about 95% of all types of kidney cancers [1]. In Europe, the incidence of kidney cancer is relatively higher, being the 8th most common cancer [2]. In a seven-year study from a single surgical center, kidney neoplasms accounted for 9% of cancer patients [3].
Minimally invasive surgery (laparoscopy, robot assisted) are the standard of care for renal tumors, even in advanced cases [4]. Nephron-sparing surgery (NSS) is a surgical technique developed over 70 years ago, aiming to reduce the unnecessary loss of renal parenchyma after resection of small masses (≤7 cm) [5]. Although several studies provided evidence that NSS is feasible in larger tumors, it remains mainly a procedure for cT1 disease. Nephron sparing surgery has shown similar disease-free survival with radical nephrectomy, but improved overall survival [6,7]. Furthermore, one of the main advantage is

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that it allows maximum preservation of non-tumoral renal parenchyma, which is important in patients with impaired renal function or at high-risk of end-stage renal disease.

Standard partial nephrectomy (SPN), a procedure that ensures an adequate safety margin of normal renal parenchyma is still considered the gold standard. However, several studies have demonstrated that the status of the resection margins is more important than the thickness. Thus, simple enucleation (SE) is used more often in order to preserve even more healthy renal tissue [8].

Simple enucleation relies on the possibility of identification of an avascular plane between the tumor pseudocapsule and renal parenchyma. Preoperative imaging is essential for operative planning, both using CT or CEUS [9]. Recent advances in intraoperative ultrasound have shown that it can enhance the delineation of renal tumor and assist simple enucleation [10]. The blunt dissection can even potentially lead to lower positive surgical margins. No difference in the oncological outcomes was reported between standard partial nephrectomy and simple enucleation. Nonetheless, an avascular plane dissection overcomes the need for arterial clamping leading to superior functional outcomes.

The leading cause of renal function impairment after partial nephrectomy is not only the quality but also the quantity of preserved nephrons. Thus, in the current study we aimed to assess whether there is a difference in the renal function after laparoscopic enucleation as compared to standard partial nephrectomy. Also, other factors were queried for their impact upon functional outcomes at 1-year follow-up.

## Material and Methods

The study was observational, longitudinal, analytical, prospective and cohort type. Consecutive patients previously diagnosed with renal cell masses who underwent laparoscopic nephron-sparing surgery in our department, between January 2015 – December 2017 were included in the present study. All patients signed the informed consent. The study protocol was in accordance with the Helsinki Declaration of 1975, as revised in 2000, and was approved by the local Ethics Committee.

The inclusion criteria were: the diagnosis of renal cell carcinoma clinical stage T1, for which laparoscopic nephron-sparing surgery (either enucleation or partial nephrectomy) was performed, patient's age over 18 years and signing the informed consent. The exclusion criteria were: patients not signing the informed consent form, patients with indication for radical nephrectomy, patients with a benign tumor.

The following clinical data were assessed: age, gender, environment, smoking status, body mass index (BMI), history of cardiac diseases (arterial hypertension, heart failure, diabetes). Tumor diameter, clinical stage of the carcinoma and the affected kidney were recorded as well. Surgery related variables included ASA score, pre- and postoperative hemoglobin (reference values 12-16 g/dl for women, 13-16.5 g/dl for men), preoperative creatinine (normal values 0.8-1.2 mg/dl), type of intervention (laparoscopic enucleation or laparoscopic partial nephrectomy) and total duration of surgery. The renal function was assessed by means of creatinine and eGFR. The glomerular filtration rate was estimated using the CKD-EPI equation for all three creatinine measurements [11]. Patients were followed for one year after surgery.

All surgeries were performed using the laparoscopic 3D technique, by either transperitoneal or retroperitoneal approach. Choice of operative technique and use of warm ischemia vs. no ischemia was dictated by tumor location and the surgeon's preference [12].

For the transperitoneal approach, the patient was placed in a 60 degress flank position and 4 trocars were used. A 10-mm trocar was inserted supraumbilical, lateral to the rectus muscle, to establish pneumoperitoneum and afterwards was used for the insertion of the 30-degree endoscope camera. CO2 was used to establish pneumoperitoneum with an intra-abdominal pressure of 10 to 14 mmHg. The other trocars were inserted only after the inspection of the peritoneal cavity and under visual control. A 10 mm trocar was placed in the midclavicular line and the other one midway between the iliac crest and umbillicus. A 5 mm trocar was inserted in the anterior axillary line for suction. The first operative step consisted in lysis of adhesions, which allowed the incision of posterior parietal peritoneum according to the line of Toldt.

After the mobilization of the colon, the ureter was identified on the anterior side of the psoas. The dissection continued cranially up to the renal pedicle. A good approach to the renal pedicle requires partial mobilization of the descendent segment of the duodenum, using blunt and gentle dissection, which allows the exposure of the anterior side of the kidney. On the left side the phrenocolic and splenocolic ligaments were divided.

After pedicle isolation, Gerota's fascia was opened depending on tumor position. Kidney mobilization allowed access and tumor margin approach. After tumor localization, the renal capsule was incised circumferentially with monopolar scissors, continuing with the dissection of the tumoral pseudocapsule. Cold dissection was used in order to respect the cleavage plane.

NSS procedures began without vessel clamping and if bleeding was important at the time of enucleation, clamping of the artery was performed so the time of warm ischemia (WIT) was reduced.

At the base of the tumor, gentle dissection was performed where the tumor meets the renal parenchyma. In case of calyceal opening, running suture with 4-0 resorbable monofilament was performed. Renorraphy was performed in a single layer using Vicryl 0 or 1, running suture secured with sliding Hem-o-lock Clips [13].

For the retroperitoneal approach, the patient was placed in a full flank position [14], with contralateral flexion. A 10-15 mm transverse incision was made in the costo-muscular angle, represented by the lateral margin of the para-vertebral muscles and the 12th rib. The working space between the psoas muscle and the kidney was developed gently using the index finger and Gaur balloon. A 10 mm trocar was inserted above the iliac crest, on the mid-axillary line. Next, the parietal peritoneum was dissected medially, creating enough space for the other trocars. The next trocar was inserted close to the antero-superior iliac spine. The fourth trocar was inserted close to the 12th rib on the anterior axillary line.. After developing the retroperitoneal space, the dissection was performed on the psoas muscle. The Gerota's fascia was incised and the ureter was identified. The dissection continued cranially up to the renal pedicle. From this step on, the surgery continued similar to the transperitoneal approach [15].

Statistical analysis was performed using MedCalc Statistical Software version 18.11.6 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2019). Quantitative variables were tested for normality using the Shapiro-Wilk test and to calculate skewness and kurtosis. Nominal variables were characterized by frequency and percentage, and continuous data were described by mean and standard deviation. Comparisons between groups were performed using the Student t test and the chi-squared test, when appropriate. Correlations between quantitative variables were assessed by Pearson's correlation. The two-way ANOVA with repeated measures test was used to determine the influence of several parameters on the evolution of glomerular filtration rate. A p value $<0.05$ was considered statistically significant.

## Results

A number of 83 patients were included in the study. Study data are summarized in Table I. Male sex was predominant and the majority of renal masses were staged as T1a. Almost two thirds of patients underwent a partial nephrectomy, and one third simple enucleation. A slight decrease in GFR (6%) was observed at 1 year after the surgery in all patients undergoing nephron-sparing surgery.

Age was negatively correlated with preoperative GFR ($r=-0.532$; $p<0.001$) and GFR recorded one year after surgery ($r=-0.330$; $p<0.001$). GFRs were not correlated with pre- and postoperative hemoglobin levels, tumor



Table I - *Demographic, clinical and lab data*

| Variables | | Characteristic |
|---|---|---|
| Age (years) (mean±standard deviation) | | 54.9±13.7 |
| Age | <65 years | 58 (69.8%) |
| | >65 years | 25 (30.1%) |
| Gender | Male | 49 (59%) |
| | Female | 34 (41%) |
| Area of origin | Rural | 24 (28.9%) |
| | Urban | 59 (71.l%) |
| BMI (kg/m2) (mean±standard deviation) | | 28.8±4.1 |
| Smoker | | 26 (31.3%) |
| Arterial hypertension | | 43 (51.8%) |
| Heart failure | | 11 (13.3%) |
| Diabetes mellitus | | 19 (22.9%) |
| Tumor size (longest measurement) (cm) (mean±standard deviation) | | 3.4±1.1 |
| T stage | 1a | 63 (76.8%) |
| | 1b | 19 (23.2%) |
| Right kidney | | 36 (43.4%) |
| Left kidney | | 47 (56.6%) |
| ASA score | 1 | 7 (8.4%) |
| | 2 | 31 (37.3%) |
| | 3 | 43 (51.8%) |
| | 4 | 2 (2.4%) |
| Preoperative hemoglobin (g/dl) (mean±standard deviation) | | 13.8±1.4 |
| Preoperative creatinine (mg/dl) (mean±standard deviation) | | 1.02±0.28 |
| Preoperative GFR (ml/min) (mean±standard deviation) | | 80.1±21.5 |
| Type of intervention | Simple enucleation | 29 (34.9%) |
| | Standard partial nephrectomy | 54 (65.1%) |
| Duration of surgery (min) (mean±standard deviation) | | 132.8±24.5 |
| Warm ischemia time for PN (min) (mean±standard deviation) | | 18.6±3.5 |
| Postoperative hemoglobin (at 24 h) (g/dl) (mean±standard deviation) | | 11.9±1.4 |
| Creatinine one year after surgery (mg/dl) (mean±standard deviation) | | 0.93±0.27 |
| GFR one year after surgery (ml/min) (mean±standard deviation) | | 75.3±22.4 |

TABLE II - *Impact of patients and procedure characteristics on eGFR at 1 year follow-up*

| Variables | | Preoperative GFR | | GFR one year after surgery | |
|---|---|---|---|---|---|
| | | Mean±SD | p | Mean±SD | p |
| Age | <65 years | 85.9±19.9 | <0.001 | 82.2±17.8 | <0.001 |
| | >65 years | 67.2±17.4 | | 61.4±14.2 | |
| Gender | Male | 78.3±17.8 | 0.4 | 66.4±18 | <0.001 |
| | Female | 82.5±26.1 | | 80.2±22.1 | |
| Area of origin | Rural | 81.1±20.3 | 0.7 | 75.6±20.3 | 0.9 |
| | Urban | 79.6±22.2 | | 75.1±23.4 | |
| Smoking status | No | 81.5±19.8 | 0.3 | 77.6±22.2 | 0.1 |
| | Yes | 76.9±25 | | 70.2±22.3 | |
| Arterial hypertension | No | 84.7±20.5 | 0.06 | 79.9±20.5 | 0.07 |
| | Yes | 75.7±21.8 | | 71±23.4 | |
| Heart failure | No | 82.1±21.4 | 0.02 | 79.8±20.2 | 0.1 |
| | Yes | 66.4±18.2 | | 62±15.8 | |
| Diabetes | No | 80±21.6 | 0.9 | 76±21.4 | 0.5 |
| | Yes | 80.2±22.1 | | 72.7±25.9 | |
| T stage | 1a | 81.3±22.3 | 0.2 | 77.7±23.1 | 0.3 |
| | 1b | 74.8±18.3 | | 65.7±16.8 | |
| Type of intervention | Standard PN | 77.3±20.2 | 0.1 | 69.9±21.7 | 0.01 |
| | Enucleation | 85.1±23.5 | | 82.4±20.4 | |

size or duration of surgery. Warm ischemia time was not associated with GFR recorded one year after surgery.

The GFR at 1 year after the surgery as compared with preoperative level was significantly higher in patients under 65 years (p<0.001), in females (p<0.001), and in patients from the enucleation group (p=0.002). Smokers, patients with heart failure or hypertensive patients were more likely to have lower values, at the threshold of statistical significance (p=0.1; p=0.1; p=0.07 respectively) (Table II).

The two-way ANOVA with repeated measures test showed a significant decrease of GFR values at one year after the surgery for patients who underwent standard partial nephrectomy as compared to enucleation group (p=0.003). Analysis also revealed that male patients had a significant decrease of GFR values at one year after the surgery, as compared with female patients (p<0.001), and that elderly patients (>65 years) were more likely to have lower GFR (p<0.001).

When the analysis considered the simultaneous influence of age, gender and type of surgery on the GFR evolution, the threshold of statistical significance was slightly crossed (p=0.2). That was partially because to the fact that men were more likely to undergo tumor enucleation than women (60% vs. 40%) (p=0.1), and elderly patients were more likely to undergo standard PN as compared with patients under 65 years (79.2% vs. 60.3%) (p=0.1).

## Discussions

The present study evaluated the dynamic of renal function one year after the laparoscopic NSS for cT1 renal cell carcinoma. Several factors that influenced the GFR were analyzed alone and as confounders. The patients' advanced age, gender and the type of surgery were identified as the most important variables that led to impaired renal function, although their influence was not independent.

Open Simple Enucleation has been demonstrated to be an oncological safe alternative to standard partial nephrectomy [16]. The first laparoscopic partial nephrectomy was performed in 1992 by Winfield [17] and 2 years later Gill et al performed the first retroperitoneal laparoscopic partial nephrectomy (RLPN) [18].

The preserved parenchyma after surgery for renal cell carcinoma is extremely important for renal function recovery. Partial nephrectomy is currently the standard treatment when dealing with T1 renal cell carcinoma, mainly because it ensures the patients better renal function preservation. The renal function declines approximately 10% after the surgery in patients with partial nephrectomy. In most cases the compensatory hypertrophy that is expected from the contralateral kidney is marginal at best. This was observed in adults, as children have a higher capacity of regeneration. The decrease is caused by the reduction of nephrons numbers or of their function, which can happen during the surgery because of ischemia caused by clamping of renal vessels.

The study data showed a 6% mean loss in GFR at one year after NSS. Patients who underwent PN exhibited a higher loss of GFR as compared to those with simple enucleation (9.5% vs. 3.2%). Antonelli et al. showed that immediately after PN there was a decrease of 11.4% in renal function, which remained unchanged for two years after the surgery [19]. Jitao et al found a reduction of 11% in renal function after PN [20]. Parekh et al. did not find a correlation between the warm ischemia time

and postoperative creatinine [21]. These data are similar to the GFR change recorded in our study in the PN group. Laparoscopic simple enucleation is a procedure associated with a good preservation of renal parenchyma, and subsequently with a smaller decrease of renal function. Most of enucleation procedures do not need isolation or clamping of the renal vessels, due to the avascular plane between the tumor pseudocapsule and rest of the kidney, meaning that the ischemia is minimal and the need of renorrhaphy is low. Dong et al. have shown that patients that underwent simple enucleation had higher GFR values after the surgery, as compared with those with PN [20].

The age of the patients in our study had an important influence on the preoperative GFR, as well as on postoperative GFR. The difference was more obvious in elderly. Several other studies revealed the same pattern after PN [22,23]. The age-associated decrease of kidney function has been described for a long time. The cause is physiological through the reduction of the glomerular capillary flow rate and of ultrafiltration coefficient. Other pathological factors, like arterial hypertension, atherosclerosis, heart failure, smoking, accelerates as well the decline of the renal function.

The GFR values decreased more abruptly in men, as compared to women, although before surgery the differences were not statistically significant. The reduction can be partially explained by the higher prevalence of cardiovascular diseases in male patients. The same influence of gender on the kidney function decline after renal surgery was described by other studies.

The study limitations were: the relative small number of patients, the short follow-up and the impossibility of assessment of the drug treatment on the renal function dynamics.

## Conclusions

3D laparoscopic enucleation of cT1 renal masses shows better functional outcomes in terms of creatinine and eGFR as compared to standard partial nephrectomy at 1-year follow-up. Age and gender of the patient are significantly correlated with renal function dynamics after nephron-sparing surgery.


## Riassunto

Lo scopo: Valutare la funzionalità renale dopo un intervento chirurgico laparoscopico risparmiatore di nefroni (NSS) e successivamente stabilire i fattori che potrebbero influenzarne la dinamica a distanza di un anno dopo l'intervento.

Metodi: Lo studio prospettico ha incluso 83 pazienti precedentemente diagnosticati con carcinoma a cellule renali sottoposti a NSS laparoscopica. Sono stati registrati numerosi dati demografici, clinici, di laboratorio chirurgici. I pazienti sono stati seguiti per un anno dopo l'intervento chirurgico.

Risultati: Lamaggior parte dei casi (63 (76,8%)) sono stati inclusi nello stadio T1a. Quasi due terzi dei pazienti sono stati sottoposti a nefrectomia parziale (PN) (54 (65,1%)). Una leggera riduzione del GFR è stata osservata 1 anno dopo l'intervento (80,1 ± 21,5 ml / min; rispettivamente 75,3 ± 22,4 ml / min) in tutti i pazienti. L'analisi univariata ha mostrato una riduzione significativa dei valori di GFR un anno dopo l'intervento chirurgico per i pazienti sottoposti a PN standard rispetto a quelli del gruppo di enucleazione (p = 0,003). I pazienti di sesso maschile hanno mostrato una riduzione significativa dei valori di GFR un anno dopo l'intervento chirurgico, rispetto ai pazienti di sesso femminile (p <0,001), e i pazienti anziani avevano maggiori probabilità di mostrare un GFR più basso. Quando si considera l'influenza simultanea di età, sesso e tipo di chirurgia sull'evoluzione del GFR, la soglia per la significatività statistica è stata leggermente superata (p = 0,2).

Conclusione: La nefrectomia parziale rispetto all'enucleazione, l'età avanzata e il sesso maschile sono associati a compromissione della funzionalità renale a un anno dopo NSS laparoscopica.


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