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CURRENT TRENDS OF NEPHRON-SPARING SURGERY FOR RENAL CELL CARCINOMA THROUGH RETROPERITONEOSCOPIC APPROACH

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PREFAȚĂ

Existența și finalizarea acestei lucrări nu ar fi fost posibilă fără efortul conjugat a unor personalități cărora le doresc să le mulțumesc pe această cale.

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Familiei și celor dragi pentru răbdare și înțelegere.

Content

PERSONAL CONTRIBUTION

Ipoteza de lucru și obiective

This work was conceived from the fact that we wanted to evaluate the possibilities of minimally invasive conservative surgical treatment in patients with localized renal; cell carcinoma which in the last decade tended to expand their indications and to gradually replace classical surgery.

Multiple variants of preoperative anatomical scores, which quantify the complexity of surgery in an attempt to give predictability to postoperative outcomes, have been developed, most commonly used are P.A.D.U.A. (preoperative aspects and dimensions used for anatomic classification), R.E.N.A.L. (R) of the tumor, and (O) rganization of the tumor in the kidney, (R) of the tumor, and (O) rganization of the tumor.). In the literature, there are numerous published studies about preoperative scores but with contradictory results, which is why we wanted to evaluate such scores applied to the population in the geographical area that the Urology Clinic of Sibiu serves.

The retroperitoneoscopic approach, although more demanding than the laparoscopic due to the narrower working space, is superior to the latter by a faster resumption of intestinal transit due to the avoidance of the peritoneal cavity and by a lower need for antialgic medication in the immediate postoperative period.

Besides the complexity of the case given the characteristics of the tumor, postoperative outcome is influenced both by experience of the surgeon and the surgical technique he uses. Based on this premise, we wanted the evaluation of partial nephrectomy results according to suture materials used during surgery.

Last but not least, being a urological center with extensive experience in open partial nephrectomy, we wanted to evaluate the results obtained through retroperitoneoscopic approach with those obtained in classical surgery.

The research objectives in the present thesis were:

1. Evaluation of preoperative prognostic scores in patients with partial nephrectomy by retroperitoneal approach for localized kidney tumors

2. Evaluation of suture materials used for renorrhaphy in patients with retroperitoneoscopic partial nephrectomy

3. Comparison of immediate intra and postoperative results of retroperitoneoscopic partial nephrectomy with open surgery

General Methodology

In order to achieve the proposed objectives, we performed observative, prospective analytical studies, which included patients admitted to the Urology Department of Academic Emergency County Hospital Sibiu between January 2010 and July 2017, who were surgically treated for renal cell carcinoma by partial nephrectomy through the retroperitoneoscopic approach.

Intraoperative parameters, intraoperative and postoperative complications classified according to Clavien-Dindo system, renal function evolution were evaluated in terms of serum creatinine glomerular filtration rate (determined preoperatively and 48 hours postoperatively).

Preoperative the following patients data were recorded:
- demographics (age, sex)
- the body mass index
- Preoperative anatomical scores (P.A.D.U.A., R.E.N.A.L. and zonal NePhRO)
- serum creatinine, along with the glomerular filtration rate estimated using the CKD-EPI formula

Intraoperatively the following data were recorded:
- the total operative time
- warm time ischemia

- suturing time of the renal parenchymal defect
- needed for suture of the collector system
- estimated blood loss

Postoperatively were followed:
- blood loss requiring transfusion
- complications based on the Clavien-Dindo system
- erum creatinine determined 48 hours postoperatively, along with the glomerular filtration rate estimated using the CKD-EPI equation
- hospital stay

The statistical analysis of this paper was performed using the chi-square test, the exact Fischer test, and the Mann-Whitney U test for parametric variables. SPSS version 18 and Microsoft Excel were also used. A $p < 0.05$ value was considered statistically significant.

Study 1 - Evaluation of preoperative prognostic scores in patients with partial nephrectomy by retroperitoneal approach for localized renal cell carcinoma

Objectives of the study

Our objective is to evaluate which of the three assessment systems is more accurate in determining the intraoperative and postoperative characteristics in patients undergoing nephron-sparing retroperitoneoscopic surgery for T1 renal tumors.

Material and method

Between January 2014 and July 2017, 37 patients (p) received nephron-sparing surgery through the retroperitoneal approach for localized renal cell carcinoma in our department. All patients had a normal contralateral kidney. Patient selection for nephron-sparing surgery was based on preoperative CT scan, tumor location, general health status of each patient and individual surgeon's preferences.

All patient data were entered into a summary table, including age, gender, preoperative anatomical preoperative assessment system P.A.D.U.A., R.E.N.A.L. and the NePhRO zonal system, operator time (from opening to closing), estimated blood loss and hospitalization period.

Surgical retroperitonescopic nepho-sparing technique

For the retroperitoneal approach we used 4 trocars, one 10 mm for the camera at the tip of the 12 rib, and onther 3 working trocars (one 10 mm and two 5 mm). After positioning the 4 trocars and creating the retroperitoneal work space, the Gerota fascia was opened and the renal artery was isolated. In order to comply with the oncological rules of the procedure the fat surrounding the tumor was excised. The renal artery was then clamped with a vascular bulldog, without clamping the renal vein, and cold excision of the renal mass using round-tipped scissor was performed.

The specimen was placed in a retriving bag, which was then removed at the end of the procedure. Interrupted 3.0 Vicryl suture was perform in order to close the collecting

system if it was injured. The renal parenchyma defect was closed with 1 Vycril running suture for 21 patients witch was locked at both tail ends with Hem-o-lock clips, and for 16 patients we used 1 V-loc running suture. After the hemostasis was complete the renal artery was unclamped.

Results

Thirty-seven patients fully met the criteria for inclusion in the study and were evaluated to achieve the objectives of this study.

The mean age of patients with partial nephrectomy was 54.3 ± 9.1 years, with a higher incidence in the 5th and 6th decades of life.

In the study, the prevalence rate was 2.3: 1 in favor of male gender. The mean serum creatinine preoperative for the patient group was 0.97 ± 0.14 mg / dl. All patients had normal contralateral kidneys. The mean tumor diameter in this group was 3.6 ± 0.86 cm.

The preoperative comparative characteristics of the patients in addition to the mean age, the tomographic tumor diameter and the risk groups according to the 3 anatomical scores taken into account are presented in Table 1.

Tabel 1. Preoperative features of patients in the study

Patients	37
Mean age (years)± SD (range)	54.3± 9.1 (26-72)
Mean pre-operative creatinine value (mg/dl) ±SD (range)	0.97±0.14 (0.6-1.3)
Average tumor diameter at CT (cm) ± SD (range)	3.6± 0.86 (1.3-6.2)
P.A.D.U.A. score	
Low (6-7)	20 (54.05%)
Medium (8-9)	13 (35.13%)
High (10-14)	4 (10.82%)
R.E.N.A.L. nephrometry score	
Low (4-6)	19 (51.35 %)
Medium (7-9)	17 (45.94 %)
High (10-12)	1 (2.71 %)
Zonal NePhRO score	
Low (4-6)	16 (43.24 %)
Medium (7-9)	11 (29.72 %)
High (10-12)	10 (27.04 %)
Average tumor volume at CT (ml) ± SD (range)	28.9±6.3(16-64)

SD- standard deviation

Following evaluation of preoperative features based on anatomical quantification systems, they had a comparable percentage of patients included in the low risk group with regard to the complexity of surgery, P.A.D.U.A. showing the highest percentage of 54.05% compared to the other two scores, which had 51.35% and 43.24%, respectively.

In the intermediate risk group the R.E.N.A.L. had the highest number of patients included with a percentage of 45.94%, followed by P.A.D.U.A. with 35.13% and NePhRO zoning with 29.72%.

A significant number of patients were included according to the NePhRO score in the high risk group of 27.04%, relative to the low percentage of the other two systems 10.82% for P.A.D.U.A. and 2.71% for R.E.N.A.L.

When using P.A.D.U.A. to assess preoperative tumor characteristics and to compare them with intraoperative and postoperative results, we notice that the operator time increases proportionally from 116.5 minutes (min) in low-risk patients to 166.2 minutes in high-risk patients with significance significant statistic demonstrated by p value less than 0.001.

The rest of the results evaluated in this study are presented in Table 2.

Tabel 2. Pre-, intra- and postoperative parameters reported in P.A.D.U.A risk classes

| | P.A.D.U.A. score | | | P value |
	Low risk	Medium risk	High risk	
Patients	20	13	4	n/a
Operative time (min) ± SD (range)	116.5±22.7 (90-170)	160.7±32.5 (95-230)	166.2±4.7 (160-170)	<0.001
Blood loss (ml) ±SD (range)	178.1±30.3 (150-250)	266.9±161.6 (150-750)	197.5±15.0 (180-210)	0.07
Transfusion rate	0	1 (2.7%)	0	n/a
Warm time ischemia (min) ±SD (range)	18.2±2.94 (14-25)	24.3±5.9 (15-39)	23.2±7.1 (14-31)	0.001
Estimated preoperative mean glomerular filtration rate (ml/min/1.73 m2) ±SD (range)	81.93±22.23 (44.56-124.91)	81.02±11.2 (61.38-96.56)	77.79±9.56 (66.88-95.72)	n/a
Postoperative mean glomerular filtration rate	75.77±18.85(40.91-108.32)	70.2±16.98(33.04-90.01)	65.24±8.91(50.14-84.77)	n/a

(48h) (ml/min/1.73 m2) ±DS (interval)				
Percentage of decrease in glomerular filtration rate after partial nephrectomy (%)	7.51%	13.35%	16.13%	0.02
Suture collection system	1 (2.7%)	12 (32.4%)	4 (10.8%)	n/a
Hospital stay	4.0±1.16(3-7)	4.2±1.18(3-7)	5.2±1.5(4-7)	0.12

The warm ischemia time ranged from 14 to 39 minutes, with a statistically significant difference between the risk classes of the P.A.D.U.A score (p 0.001).

The estimated glomerular filtration rate using the CKD-EPI equation decreased slightly, the P.A.D.U.A. and the average percentage drop was 7.51% for low risk, respectively 13.35% and 16.13% for medium and high risk (p = 0.0252).

The same batch of patients was evaluated using the preoperative anatomical pre-operative rheumatoid arthritis score. The evaluated characteristics are listed in Table 3.

Tabel 3. Pre-, intra- and postoperative parameters reported to R.E.N.A.L.

	R.E.N.A.L. (nephrometric score)			P value
	Low risk	Medium risk	High risk	
Patients	19	17	1	n/a
Operative time (min)± SD (range)	118.4±21.7(90-170)	164.4±33.4(120-230)	160	0.02
Blood loss (ml) ±SD (range)	171.1±24.9(150-230)	257.6±140.5(170-750)	190	0.04
Transfusion rate	0	1 (2.7%)	0	n/a
Warm time ischemia (min) ±SD (range)	17.6±2.7(14-25)	23.9±5.5(14-39)	31	<0.001
Estimated preoperative mean glomerular filtration rate (ml/min/1.73 m2) ±SD (range)	78.49 ± 8.44 (44.56-104.45)	80.22 ± 21.45 (0.7-13)	66.88	n/a
Postoperative mean glomerular filtration rate (48h) (ml/min/1.73 m2) ±DS (interval)	77.31±16.23(40.91-108.32)	72.89±23.91(33.04-106.67)	50.14	n/a

Percentage of decrease in glomerular filtration rate after partial nephrectomy (%)	1.5 %	9.13 %	25.02 %	0.006
Suture collection system	0	16 (43.2 %)	1 (2.7%)	n/a
Hospital stay	3.9± 1.11(3-7)	4.2± 1.14(3-7)	7	0.04

R.E.N.A.L. nephrometry score was able to predict warm ischemia according to the risk groups (17.6 vs 23.9 vs 31 min) with a p value below 0.001.

Decreased renal function was directly proportional to the score, 1.5% in the low risk group, 9.13% and 25.02% in the medium and high risk patients (p = 0.006).

The zonal NePhRO score was statistically correlated with total operative time, blood loss, warm ischemia time, and decreased renal function, all with p <0.05 (Table 4)

Tabel 4. Parametrii pre-, intra- și postoperatori raportați la clasele de risc NePhRO

	Zonal NePhRO score			P value
	Low risk	Medium risk	High risk	
Patients	16	11	10	n/a
Operative time (min)± SD (range)	128.1±24.8(90-170)	131.3±29.7(90-170)	171.0±25.1(140-230)	<0.001
Blood loss (ml) ±SD (range)	181.8±29.9(150-250)	180.0±34.6(140-250)	293.0±175.7(170-750)	0.009
Transfusion rate	0	0	1 (2.7%)	n/a
Warm time ischemia (min) ±SD (range)	18.5±3.3(14-25)	19.3±3.9(14-26)	26.5±5.9(20-39)	<0.001
Estimated preoperative mean glomerular filtration rate (ml/min/1.73 m2) ±SD (range)	90.57±19.51 (56.45-124.91)	70.28±11.47 (44.56-95.72)	78.08±13.45 (0.8-96.56)	n/a
Postoperative mean glomerular filtration rate (48h) (ml/min/1.73 m2) ±DS (interval)	88.06±18.45 (62.41-108.32)	66.09±8.33(40.91-84.77)	63.24±19.54(33.04-96.56)	n/a
Percentage of decrease in glomerular filtration rate after partial nephrectomy (%)	2.77 %	5.96 %	19.00 %	0.002

| Suture collection system | 2 (12.5%) | 5 (45.4%) | 10 (100%) | n/a |
| Hospital stay | 4.1±1.2 (3-7) | 3.7±1.13 (3-7) | 4.7±1.26 (3-7) | 0.11 |

The zonal NePhRO score was able to make a statistically significant breakdown of warm ischemia, increasing proportionally from 18.5 min on average to low risk, 19.3 min at intermediate risk and 26.5 min at risk high.

Also, in predicting the decrease in glomerular filtration rate over the postoperative period, this quantification system has managed to isolate difficult cases in the high risk group, with a 19% decrease compared to 2.77% in the low risk group.

All intraoperative and postoperative complications were recorded and classified according to the Clavien-Dindo system. Following nine-fold nephro-sparing surgery, nine patients (24.3%) developed subcutaneous emphysema and one patient (p) (2.7%) required intra-operative blood transfusions. Postoperative complications were urinary fistula in a patient requiring a double ureteral stent J, a patient with post-operative bleeding who received blood transfusions, two patients with antibiotic-treated urinary tract infections, and two patients treated with Clostridium difficile with oral antibiotics and parenteral hydro-electrolytic rebalancing (Table 5).

Tabel 5. Intra- and postoperative complications - low risk

Complications	Low risk		
	P.A.D.U.A	R.E.N.A.L	NePhRO
Subcutaneous emphysema	3 (8.1 %)	2 (5.4%)	3 (8.1 %)
Intraoperative bleeding requiring transfusion	0	0	0
Infection with Clostridium difficile	1 (2.7%)	1 (2.7%)	1 (2.7%)
Urinary tract infections	0	0	0
Urinary fistula	0	0	0
Postoperative bleeding requiring transfusion	0	0	0
hematoma	0	0	0
Clavien-Dindo Classification			

Grade I	3 (8.1 %)	2 (5.4%)	3 (8.1 %)
Grade II	1 (2.7%)	1 (2.7%)	1 (2.7%)
Grade III	0	0	0
Grade IV	0	0	0
Grade V	0	0	0
Total	4 (10.8 %)	3 (8.1 %)	4 (10.8 %)

The complication rate was 51.1%, mostly in the 1st and 2nd grades. Within the average risk group, 2 patients (5.4%) of the subgroup bounded by the R.E.N.A.L. score, and according to the other two scores only 1 patient (2.7%) presented grade III complications. (Table 6)

Tabel 6. Complicaţii intra- şi postoperatorii - risc mediu

Complications	Medium risk		
	P.A.D.U.A	R.E.N.A.L	NePhRO
Subcutaneous emphysema	5 (13.5%)	7 (18.9%)	3 (8.1 %)
Intraoperative bleeding requiring transfusion	1 (2.7%)	1 (2.7%)	0
Infection with Clostridium difficile	0	0	0
Urinary tract infections	2 (5.4%)	2 (5.4%)	2 (5.4%)
Urinary fistula	1 (2.7%)	2 (5.4%)	1 (2.7%)
Postoperative bleeding requiring transfusion	1 (2.7%)	1 (2.7%)	0
hematoma	1 (2.7%)	1 (2.7%)	0
Clavien-Dindo Classification			
Grade I	5 (13.5%)	7 (18.9%)	3 (8.1 %)
Grade II	5 (13.5%)	5 (13.5%)	2 (5.4%)
Grade III	1 (2.7%)	2 (5.4%)	1 (2.7%)
Grade IV	0	0	0
Grade V	0	0	0

| Total | 11(29.7%) | 14 (37.8 %) | 6 (16.2%) |

The highest rate of complications in the high-risk subgroup was assessed by patients evaluated with the NePhRO score of 24.3%, one patient compared to P.A.D.U.A. and NePhRO being a Grade III complication according to the Clavien-Dindo classification. (Table 7)

Tabel 7. Intra-and postoperative complications - high risk

Complications	High risk		
	P.A.D.U.A	R.E.N.A.L	NePhRO
Subcutaneous emphysema	1 (2.7%)	0	3 (8.1 %)
Intraoperative bleeding requiring transfusion	0	0	1 (2.7%)
Infection with Clostridium difficile	1 (2.7%)	1 (2.7%)	1 (2.7%)
Urinary tract infections	0	0	0
Urinary fistula	1 (2.7%)	0	1 (2.7%)
Postoperative bleeding requiring transfusion	1 (2.7%)	1 (2.7%)	2 (5.4%)
hematoma	0	0	1 (2.7%)
Clavien-Dindo Classification			
Grade I	1 (2.7%)	0	3 (8.1 %)
Grade II	2 (5.4%)	2 (5.4%)	5 (13.5%)
Grade III	1 (2.7%)	0	1 (2.7%)
Grade IV	0	0	0
Grade V	0	0	0
Total	4 (10.8 %)	2 (5.4%)	9 (24.3%)

Of the three preoperative anatomical quantification systems, the NePhRO score showed the highest rate in the high risk group of 24.3%, compared to the R.E.N.A.L. and P.A.D.U.A. who showed the highest rate within the intermediate risk group of 37.8% and 29.7%, respectively.

Discussions

All patients in the study benefited from nephron-sparing surgery for renal tumors and were evaluated before surgery using three different scoring systems: P.A.D.U.A., R.E.N.A.L. nephrometry and the zonal NePhRO system.

The population included in our study had an average age of 54.3 years with a standard deviation of 9.1 years, being comparable to literature data. Ouzaid et al. conducted a study in 2012 that included 87 patients with retroperitoneoscopic partial nephrectomy who had an average age of 59 years with a standard deviation of 11 years. This can be explained by the high prevalence of kidney carcinomas (clear cells, papillary cells or cellular chromosomes) that represent over 90% of renal neoplasms and which are specific to decades 5 and 6. [19,102]

We also observed a significantly higher percentage of male patients in the study, the M: F ratio being 2.3: 1. The same Ouzaid et al. obtained in the above mentioned study a ratio of 2: 1, and at our country this rate is 1.8: 1, which can give us terms of comparison with the literature studies, but can at the same time allow extrapolating our national results. This incidence can be explained by the increased prevalence of smoking and exposure to carcinogenic substances among men [14,102]

The mean tumor diameter of the renal cell carcinoma studied was 3.6 cm, significantly higher than those reported by Ouzaid et al. of 2.64 cm or by Reifsnyder et al. 2.6 cm. This can be explained by a slightly delayed diagnosis of renal neoplasm due to the lower access of the population of our country to advanced imaging methods (computed tomography or magnetic resonance) compared to the European average. [102,103]

Warm ischemia time is the most important aspect of nephro-sparing surgery, with a major influence on postoperative renal function. The score of R.E.N.AL. and the NePhRO score could accurately predict the time of ischemia, with a p value of <0.001.

When comparing the two evaluation systems in terms of wram ischemia, the value varies from 17.6 min versus 18.5 min to low risk tumor characteristics, up to 23.9 min versus 19.3 min at those with medium risk and 31 versus 26.5 min for high risk tumor. Score P.A.D.U.A. has a p value of 0.001, but with respect to the mean time of warm ischemia, it was unable to differentiate between the medium and the high risk group. An important component of the NePhRO quantification system is the infiltration of the

collector system, which is an independent factor in predicting the time of warm ischemia time. This is most likely due to the need for suture of the collecting system, which significantly prolongs the time.

The results are comparable to those previously reported in different series of patients undergoing partial nephrectomy. [101.104-107]

Another important aspect of nephro-sparing surgery is the glomerular filtration rate (GFR) after the procedure. We estimated the GFR rate using the CKD-EPI equation, which provides impartial and fairly accurate estimates for a wide range of subgroups [108], serum creatinine determined one day before the procedure and 48 hours after surgery .

The NePhRO zonal score achieved the strongest statistical correlation in terms of decreasing the estimated GFR rate, with a p value of 0.002, while P.A.D.U.A. and R.E.N.A.L. recorded a p value of 0.006 and 0.02, respectively.

R.E.N.A.L. evaluation system was the only one that had statistical relevance in terms of duration of hospitalization, with a p value of 0.04.

All three assessment systems were able to predict complications after surgery, with statistical significance in the Grade III group according to the Clavien-Dindo classification, with a p value of <0.005, comparable to data reported by Hakky et al. [101].

The limits of our study are the lack of long-term postoperative assessment and the reduction in the number of cases over time, as the partial laparoscopic nephrectomy (LPN) intervention is practiced in our department in January 2014.

Conclusions

P.A.D.U.A., R.E.N.A.L. nephrometry and zonal NePhRO scores have been proven to be preoperative reliable tools to assess surgical complexity and to predict outcome such as warm ischemia, blood loss, estimated postoperative GFR rate, and complication rate.

These evaluation systems are not ideal, leaving room for research to find a more objective formula that excludes subjective features such as surgeon's experience in achieving a more accurate result.

Study 2 - Evaluation of Suture Materials Used for Renorrhaphy in Patients with Retroperitoneoscopic Partial Nephrectomy

Objectives of the study

Since the first surgical procedures, the suture materials have been an indispensable tool in the surgeon's armamentarium, with a continuous evolution from the plant and animal origin to the synthetic composition.

According to literature data, both the polidioxanone unidirectional suture thread (V-Loc™) and the polyglycolic acid (Bicril ™) are absorbable sutures suitable for closing the renal parenchymal defect following nephron-sparing surgery, with similar results intraoperative blood loss, complication rate, and duration of hospitalization.

Material and method

In the present study we analyzed the intraoperative and postoperative outcomes of patients on whom partial nephrectomy was performed for T1 renal neoplasm and where V-LocTM (Covidien) or BicrilTM (Biosintex) were used to close the renal parenchymal defect.

We analyzed 37 consecutive patients between January 2014 and July 2017, who received nephron-sparing surgery for T1-T2 renal tumors. We divided the patients into 2 groups according to suture materials used for renorrhaphy, Bicril™ 1 suture for 21 patients, used as a continuous suture that was secured at both ends with Hem-o-lockTM clips, and for 16 patients we used V-loc™ 1 for continuous suturing.

For a more objective assessment, we divided patients into 3 subgroups according to the risk group determined by zonal NePhRO preoperative scoring system.

We have compiled a summary table of age, sex, anatomical preoperative assessment system, operative time (from opening to closing), estimated blood loss, warm ischemia, and hospitalization duration.

Perioperative complications were carefully classified using the Clavien-Dindo system.

The statistical analysis of this study was performed using the chi-square test, the exact Ficher test and Microsoft Excel functions. P <0.05 was considered statistically significant.

Results

The mean age of patients with partial nephrectomy was 54.3 ± 9.1 years. The mean serum creatinine preoperative for the patient group was 0.97 ± 0.14 mg / dl. All patients had normal contralateral kidneys. The mean tumor diameter in this group was 3.6 ± 0.86 cm. All features are presented in Table 8.

Tabel 8. Intra- and postoperative parameters for low-risk patients

	Low-risk zonal N-PLRO score (4-6)		P value
	Minor Group	Major Group	
Patients	7	9	n/a
Operative time (min)± S D (range)	108.5±14.0(95-135)	143.3±20.3 (110-170)	<0.001
Estimated blood loss (ml) ±SD (range)	165.7±21.4 (150-170)	194.4±30.8 (160-250)	0.004
Warm ischemia time (min) ±SD (range)	16.0±3.0 (14-18)	18.2±2.03 (17-25)	0.02
Collecting system suture	0	2 (22.2 %)	n/a
Hospital stay	3.42±0.6 (3-4)	4.6±1.3(3-7)	0.07

In patients with a zonal NePhRO score of 4-6, the type of suture used for renorrhaphy showed a strong statistical correlation with total operative time (p <0.001), estimated blood loss (p = 0.004) and warm ischemia time (p = 0.02). Within this subgroup, 2 patients (22.2%) required the suture of the collecting system, both of which were part of the Bicril™ patient population.

The mean time of warm ischemia was 12.3% shorter in the batch using the unidirectional polidioxanone suture versus the polyglycolic acid group.

Concerning the average risk group, warmer ischemia was significantly shorter in the V-loc™ suture group than in the Bicril ™ group (17.7 min vs 20.8 min) with a p value of 0.001, but when we introduced the suture of the collection system that prolongs the ischemic time, the p value increased to 0.05, being at the limit of statistical significance.

The percentage of warm ischemia in total operative time is comparable between the two groups

The average operative time was 115.5 minutes for the V-loc group, while for the Bicril group it was 17.9% longer, being 140.7 minutes.

The rest of the results are presented in Table 9 and are comparable to the low-risk group, except for the length of hospitalization, which becomes statistically relevant.

Tabel 9. Parametrii intra- și postoperatorie pentru pacienții cu risc mediu

	Median risk zonal NePhRO score 4-6		P value
	V-loc™ Group	Bicril™ Group	
Patients	4	7	n/a
Operative time (min)± S D (range)	115.5±21.8 (90-165)	140.7±23.7 (105-170)	<0.001

Estimated blood loss (ml) ±SD (range)	165.0±38.4(140-210)	188.5±84.1 (150-250)	0.1
Warm ischemia time (min) ±SD (range)	17.7±2.94 (16-22)	20.8±3.1 (14-24)	0.001
Collecting system suture	1 (25%)	4 (57.1%)	n/a
Hospital stay	3.2±0.4(3-4)	4.0±0.8(3-5)	0.04

The high risk group is the most representative for this study because there are no major differences between patients influencing the statistical analysis, all patients requiring the suture of the collection system.

Both the operative time and estimated blood loss were higher in the Bicril™ group compared to the V-loc™ group, 184.0 minutes versus 158.0 minutes and 344.0 ml versus 242.0 ml with a p < 0.001 and 0.01 respectively. (Table 10)

Tabel 10. Intra- and postoperative parameters for high-risk patients

	Medium-risk zone PNSPHIRO score (4-6)		P value
	V-loc TM Group	Bicril TM Group	
Patients	5	5	n/a
Operative time (min)± SD (range)	158.0±21.1 (140-170)	184.0±29.9 (160-230)	<0.001
Estimated blood loss (ml) ±SD (range)	242.0±125.7 (170-400)	344.0±232.3 (190-750)	0.01
Warm ischemia time (min) ±SD (range)	22.2±3.1 (20-26)	30.8±5.4 (25-39)	<0.001
Collecting system suture	5 (100%)	5 (100%)	n/a
Hospital stay	4.0±0.7 (3-5)	5.4±1.0(4-7)	0.009

Warm ischemia time was significantly lower in the V-loc™ patient group, with a 28% lower than the Bicril™ suture, with a p value below 0.001.

Discussions

Our study demonstrated the efficacy of the unidirectional polydioxanone suture in order to close the renal parenchymal defect, achieving superior results in the time of warm ischemia to the polyglycolic acid suture.

Several authors reported a significant reduction in the time of warm ischemia for patients using unidirectional suture for renorraphy [115,116,117], which correlates with our results, V-loc™ suture reducing the ischemic time by 27.9% compared to Bicril™ suture.

Knowing that continuous suture reduces the time of warm ischemia irrespective of tumor size and location [113], and that tightening of the nodule on which the laparoscopic takes time and is often weaker than manual binding in open surgery [111,112,114] for nephron-sparing surgery through the retroperitoneal approach (which offers a reduced space of maneuver), and based on the results obtained in the study, we can appreciate that the continues suture without knots, using the Hem-o-lock™ suture clips is a festive technique can significantly improve postoperative outcomes, and in particular reduce the risk of renal damage in the postoperative period.

Both suture materials used for kidney parenchyma suture have good results in biodegradability [111,119], suture requiring good traction resistance over a month to maintain good hemostasis and facilitate kidney healing. Another important problem is the bacterial adherence that appears to favor the use of polidioxanone thread over polyglycolic acid [120].

The end-to-end loop V-loc™ design provides the surgeon the ability to perform a knot-free suture with a single Hem-o-lockTM clamp placed at the end of the suture,

reducing the cost of surgery compared to the technique where multiple clips are required Hem-o-lock™, these devices representing an effective fastening system according to Grigore et al. [118]

Conclusions

The V-locTM suture is a safe unidirectional suture which allows the urologist surgeon to perform a quality suture in the renal parenchymal defect after excision of the tumor, while reducing the time of warm ischemia and obtaining good hemostasis in nephron-sparing surgery compared to standard absorbable suture.

Through the intraoperative comfort provided to the urologist, along with the good intraoperative and postoperative results, he is currently positioning the unidirectional suture suture in an important place between the suture materials used in the partial nepherectomy through the retroperitoneopic approach.

Large-scale prospective studies with long-term follow-up and direct comparison with newly emerging sutures are needed to confirm the place of unidirectional sutures in the urologist's armamentarium.

Study 3 - Comparison of Immediate Intra and Postoperative Outcomes of Retroperitoneoscopic Partial Nonprectomy with Open Surgery

Objectives of the study

Open partial nephrectomy (OPN) was the standard gold treatment for small-sized kidney tumors in the first decade of the 21st century [121]. Partial laparoscopic nephrectomy (PLN) tends to replace OPN due to similar oncological results, decreased postoperative anti-algic medication use, short hospital stay and short convalescence [122].

The objective of the study is the comparative evaluation of two surgical techniques of partial nephrectomy, retroperitoneoscopic and open surgical approach in the treatment of T1-T2 renal cell carcinoma.

Material and method

Between January 2010 and February 2017, 76 patients benefited from partial nephrectomy for clinically located renal tumors, 37 patients benefited from LPN by retroperitoneoscopic approach and 39 patients through open surgery (OPN). Patient selection for nephron-sparing surgery was performed on a preoperative CT scan, tumor location, individual biological status, and individual surgeon preference.

We have compiled a summary retrospective table, which included age, patient sex, nephrometric score, operative time (from opening to closure), estimated blood loss, warm ischemia, duration of hospitalization, pathological stage and surgical margins.

Perioperative complications were carefully classified using the Clavien-Dindo system.

An evaluation of the classification of complications and the calculation of the nephrometric score were performed by 3 persons.

LPN was achieved by retroperitoneal approach. After positioning the 4 trocar and creating the retroperitoneal workspace, the Gerota fascia was opened and the renal artery was isolated. To comply with the oncological rules of the procedure, the fat surrounding the tumor was excised. The renal artery was then clamped with a vascular bulldog without renal vein clamping, and cold renal excretion was performed using round-tipped scissors.

The specimen was placed in a recovery bag, which was then removed at the end of the procedure. 3.0 Bicril™ interrupted suture was used to close the collection system when involved. The 3.0 Bicril™ suture for interrupted suture was used in renal parenchyma repair in order to obtain segmental artery hemostasis. The renal parenchymal defect was closed with a continuous suture of polyglycolic acid 1 or polyidioxanone (V-loc™) 1, provided at both ends with Hem-o-lock clips. After hemostasis, the renal artery was unclamped.

For OPN, after clamping of the renal artery, the tumor was excised, then the collection system was sutured with 3.0 Bicril ™ - discontinued suture. Renal parenchyma

was closed with a discontinued suture with polyglycolic acid 1, with or without the use of haemostatic agents (Gelaspon ™).

Results

The mean age of patients with partial nephrectomy was 59.6 ± 16.4 years, with 57.9 ± 11.6 years for the subgroup with laparoscopic partial nephrectomy and 61.3 ± 12.4 for open surgery. Preoperative serum creatinine was the same for both patient groups.

Regarding tumor localization, the results are comparable between the group with laparoscopic partial nephrectomy and the one with open partial nephrectomy.

Patients in the OPN group had larger tumors and high nephrometric scores and P.A.D.U.A. scores.

The patient's preoperative comparative characteristics are presented in Table 1.

Tabel 11 Preoperative features of patients in the study

	All patients	LPN	OPN	p
Patients	76	37	39	
Mean age (years)± SD (range)	59.6± 16.4 (29-76)	54.3± 9.1 (26-72)	61.7±12.4(32-76)	ns
Preoperative mean serum creatinine (mg/dl) ±SD (range)	1.0±0.4 (0.7-1.5)	0.97±0.14 (0.6-1.3)	1.0±0.4 (0.7-1.5)	ns
Side of tumor				
Right	28 (36.8%)	16 (43.2%)	12 (30.7%)	ns
Left	48 (63.2%)	21 (56.8 %)	27 (69.3%)	ns
Tumor lacalization				
Upper pole	20 (26.3%)	10 (27.0 %)	10 (25.6 %)	ns
Mediorenal	19 (25.0 %)	8 (21.6%)	11 (28.2 %)	ns
Lower pole	37 (48.7%)	19 (51.4)	18 (46.2 %)	ns
Average tumor diameter at CT (cm) ± SD (range)	3.7± 1.42(1.3-6.7)	3.6± 0.86 (1.3-6.2)	4.1±1.9(1.5-6.7)	ns
P.A.D.U.A. score				
Low (6-7)	39 (51.3 %)	20 (54.0%)	19 (48.7 %)	ns
Medium (8-9)	24 (31.5 %)	13 (35.1%)	11 (28.2%)	ns
High (10-14)	12 (17.2 %)	4 (10.9%)	8 (23.1%)	ns
R.E.N.A.L. nephrometry score				
Low (4-6)	41 (53.9 %)	19 (51.4 %)	22 (56.4 %)	ns

Medium (7-9)	26 (34.2 %)	17 (45.9 %)	9 (20.5 %)	ns
High (10-12)	9 (11.9 %)	1 (2.7 %)	8 (23.1 %)	ns
Average tumor volume at CT (ml) ± SD (range)	34.1±19.7(16-68.1)	28.9±6.3(16-57.4)	40.2±17.2 (19.3-68.1)	ns

LPN-laparoscopic partial nephrectomy, OPN-open partial nephrectomy, SD- standard deviation

In the studied group, 48.7% of the tumors were localized to the lower renal pole, while 63.2% of the renal neoplasms were located in the left kidney.

In our study, mean operator time was longer for the LPN group 140.6 minutes vs. 98.6 minutes for the OPN group, while estimated blood losses were lower in the LPN group (211.3 ml vs. 324.5 ml). (Table 12)

Tabel 12 Intra- and postoperative features

	All patients	LPN	OPN	
Patients	76	37	39	
Operative time (min)± SD (range)	117.9±41.4(75-230)	140.6±31.9(90-230)	98.6±19.8(75-140)	0.002
Estimated blood loss (ml) ±SD (range)	245.4±175.6(100-750)	211.3±88.6(100-750)	324.5±162.3(210-500)	0.031
Transfusion rate	3.9 % (3/76)	8.1 %(3/37)	0 %	n/a
Warm ischemia time (min) ± SD (range)	19.4±9.1(15-39)	20.9±5.4(19-39)	15.4±2.9(15-23)	<0.001
Mean postoperative serum creatinine (48h) (mg/dl) ±SD (range)	1.2±0.5(0.8-1.8)	1.0±0.3(0.8-1.4)	1.3±0.6(0.9-1.8)	0.03
Collecting system suture	36 (47.3%)	17 (45.9%)	19 (48.7 %)	<0.001
Hospital stay	4.8±2.6(3-9)	4.1± 1.9(3-7)	5.3±2.7(4-9)	0.042

LPN-laparoscopic partial nephrectomy, OPN-open partial nephrectomy, SD- standard deviation, n/a – not applicable

The transfusion rate was 8.1% in the LPN group, while in the OPN group transfusion was not required. Warm ischemia time was higher in the LPN group (20.9 ±

5.4 minutes) than in the OPN group (15.4 ± 2.9). The percentage of patients who required the suture of the collection system in the two groups was approximately the same.

Complications were divided into subgroups: intraoperative and postoperative complications and are presented in Table 13. The rate of postoperative complications is comparable between LPN and OPN groups (23.81% vs. 19.47%). In the group of patients with retroperitoneoscopic approach, the rate of intraoperative complications was 27.0%, while in the OPN group there were no intraoperative events. In the LPN group, 10 patients experienced intraoperative complications, of which 9 had developed subcutaneous emphysema that resolved spontaneously and completely 24 hours postoperatively.

The rate of post-operative infection with Clostridium difficile was comparable between the two groups but with several urinary tract infections in the OPN group (7.6% vs. 5.4%). The rate of complications, including urinary fistula, wound infection, bleeding and hematoma are shown in Table 13.

Tabel 13 – Distribution of intra- and postoperative complications

Complications	OPN	LPN	Total	p
Intraoperative	0	10 (27.0%)	10 (13.1%)	
Subcutaneous emphysema	0	9 (24.3%)	9 (11.8%)	n/a
Bleeding requiring transfusion	0	1 (2.7%)	1 (1.3%)	0.9
Postoperative	7 (17.9%)	9 (24.3%)	16 (21.0%)	
Clostridium difficile infection	1 (2.5%)	2 (5.4%)	3 (3.9 %)	0.8
Wound infections	2 (5.1%)	0	2 (2.6%)	n/a
Urinary tract infections	3 (7.6%)	2 (5.4%)	5 (6.5%)	0.7
Urinary fistula	0	2 (5.4%)	2 (2.6%)	n/a
Bleeding requiring transfusion	0	2 (5.4%)	2 (2.6%)	n/a
Hematoma	1 (2.5%)	1 (2.7%)	2 (2.6%)	0.7
Total	7 (17.9%)	19 (51.3%)	26 (34.2%)	

LPN-laparoscopic partial nephrectomy, OPN-open partial nephrectomy, n/a – not applicable

Using the Clavien-Dindo classification system to evaluate the complications of the OPN group versus the LPNgroup, in our patient series, the grade 1 complications rate was 0 vs 24.3%, the grade 2 complication rate was 23, 5% versus 23.8%, and the Grade 3 complication rate was 0 vs. 8.1%. Within the study group there were no grade IV and V complications according to the Clavien-Dindo classification.

Discussions

In our patient population, more complex kidney tumors were treated by open surgery due to better intraoperative control and surgeon comfort on this approach.

All patients in the present study received partial nephrectomy with warm ischemia. The warm ischemia time was higher in the LPN group (21.9 minutes vs. 15.4 minutes), mainly due to the high-time intracorporeal suture.

The mean diameter of the renal tumor was higher in the OPN group (4.1 cm vs. 3.6 cm), due to the choice of cases with a lower complexity score for the laparoscopic and retroperitoneoscopic approach, the tumor diameter being one of the stratification criteria both for the PADUA score as well as for the R.E.N.A.L.

When considering all the features mentioned in P.A.D.U.A. and R.E.N.A.L. the scores obtained had a direct influence on the intraoperative and postoperative results, with a longer time for ischemia and a significant loss of intraoperative blood for tumors with mean and high scores with a p <0.001.

LPN has been shown to be a technical alternative to open partial nephrectomy with surgical efficiency and similar oncology results. When comparing the LPN complication rate with OPN, the literature results are divided, studies showing a rate of higher complications in the LPN group [6,7,8] and others in the OPN group [9,10].

In our study, the total complication rate is higher in the LPN group by 52.3% vs. 23.4%, but if we exclude the first degree complications, the rate is similar for both laparoscopic and open partial nephrectomy.

Urinary fistula was present in the LPN group at a rate of 5.4% (2/36) for tumors of medium and high complexity, comparable to studies in the literature that reported urinary fistula in between 3.1% and 3.4% [6,11].

The limits of our study are its retrospective nature and the lack of long-term postoperative assessment. Another limitation is the reduced number of cases over time, as LPN is practiced in our January 2014 department.

Conclusions

Laparoscopic partial nephrectomy for renal cell carcinoma is superior to open surgery by early mobilization of the patient, low rate of wound complications, short duration of hospitalization, rapid socio-professional reintegration of the patient despite the perioperative complication rate that is greater than that of open surgery but low grade according to the Clavien-Dindo classification.

Evaluation systems P.A.D.U.A. and R.E.N.A.L. can help the surgeon choose the best approach, which can lead to good oncology results with a low rate of complications.