



UNIVERSITÀ
DEGLI STUDI
FIRENZE

FLORE

Repository istituzionale dell'Università degli Studi di Firenze

Partial Nephrectomy in Clinical T1b Renal Tumors: MulticenterComparative Study of Open, Laparoscopic and Robot-

Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

Original Citation:

Partial Nephrectomy in Clinical T1b Renal Tumors: MulticenterComparative Study of Open, Laparoscopic and Robot-assisted Approach (theRECORdProject) / Porpiglia, F; Mari, A; Bertolo, R; Antonelli, A; Bianchi, G; Fidanza, F; Fiori, C; Furlanmorgia, G; Novara, G; Rocco, B; Rovereto, B; Serni, S; Simeone, C; Carini, M; Minervini, A. - In: UROLOGY. - ISSN 0090-4295. - STAMPA. - 89:(2016), pp. 45-53.
[10.1016/j.urology.2015.08.049]

Availability:

This version is available at: 2158/1054411 since: 2021-01-19T23:16:29Z

Published version:

DOI: 10.1016/j.urology.2015.08.049

Terms of use:

Open Access

La pubblicazione è resa disponibile sotto le norme e i termini della licenza di deposito, secondo quanto stabilito dalla Policy per l'accesso aperto dell'Università degli Studi di Firenze (<https://www.sba.unifi.it/upload/policy-oa-2016-1.pdf>)

Publisher copyright claim:

Conformità alle politiche dell'editore / Compliance to publisher's policies

Questa versione della pubblicazione è conforme a quanto richiesto dalle politiche dell'editore in materia di copyright.

This version of the publication conforms to the publisher's copyright policies.

(Article begins on next page)

Partial Nephrectomy in Clinical T1b Renal Tumors: Multicenter Comparative Study of Open, Laparoscopic and Robot-assisted Approach (the RECORD Project)

Francesco Porpiglia^a, Andrea Mari^b, Riccardo Bertolo^a, Alessandro Antonelli^c, Giampaolo Bianchi^d, Francesco Fidanza^d, Cristian Fiori^a, Maria Furlan^c, Giuseppe Morgia^e, Giacomo Novara^f, Bernardo Rocco^g, Bruno Rovereto^h, Sergio Serni^b, Claudio Simeone^c, Marco Carini^b, Andrea Minervini^b,

Objective

To evaluate perioperative results of open (OPN), laparoscopic (LPN), and robot-assisted partial nephrectomies (RAPN) and to identify predictive factors of Trifecta achievement for clinical T1b renal tumors in a multicenter prospective dataset.

Methods

Data of 285 patients who had OPN (133), LPN (57), or RAPN (95) for cT1b renal tumors were extracted from the RECORD Project. High-volume centers were defined as ≥ 50 overall cases of partial nephrectomy per year. Trifecta was defined as simultaneous absence of perioperative complications, negative surgical margins, and ischemia time < 25 minutes.

Results

The 3 groups had comparable body mass index, preoperative hemoglobin, creatinine and estimated glomerular filtration rate, tumor clinical diameter, and growth pattern. LPN and RAPN were more frequently exclusive of high-volume centers. RAPN showed significantly lower median estimated blood loss compared with OPN and LPN. Trifecta was achieved in 62.4%, 63.2%, and 69.5% of OPN, LPN, and RAPN ($P = \text{NS}$) cases. Median warm ischemia time (WIT) was significantly shorter during OPN than during LPN and RAPN. RAPN had significantly shorter WIT compared with LPN. RAPN was significantly less morbid than OPN regarding intraoperative and postoperative complications. LPN (1.9%) and RAPN (2.5%) showed a lower rate of positive margins compared with OPN (6.8%) ($P = \text{NS}$). At multivariable analysis, exophytic tumor growth pattern, estimated blood loss, and high-volume centers were significant predictive factors for Trifecta achievement.

Conclusion

Clinically, T1b renal tumors suitable for NSS can be safely treated by LPN or RAPN in high-volume centers. RAPN allows for significantly lower WIT and estimated blood loss with higher rate of Trifecta achievement compared with LPN.

Partial nephrectomy (PN) is nowadays strongly recommended by international guidelines when considering surgical treatment of small renal masses cT1 staged.^{1 and 2} Goals of PN are negative

cancer margin, minimal renal functional decrease, and avoidance of complications. In latest years, these goals are together constituting “Trifecta”, a concept taken from radical prostatectomy's literature now introduced in surgery for renal cancer to standardize reporting of PN outcomes. Trifecta is achieved when warm ischemia time (WIT) less than 25 minutes, negative surgical margins, and no perioperative complications are simultaneously realized.^{3, 4 and 5} For many years, open PN (OPN) has been considered the “gold standard” but since advancements in laparoscopic techniques, equipment, and operator skills, laparoscopy has been becoming more and more commonly used,² as offering comparable oncological outcomes, less morbidity, and shortened convalescence.^{2, 6, 7, 8 and 9} As such, for clinical T1a lesions, surgical removal choosing a minimally invasive approach is nowadays well established.

In patients with larger renal masses, the role of PN is less well established. In fact, European Association of Urology Guidelines support routine use of nephron sparing surgery (NSS) also for T1b tumors as it affords conservation of normal renal parenchyma, even preserving oncologic efficacy. Conversely, American Urological Association Guidelines support radical nephrectomy as standard of care in patients with major comorbidity or high surgical risk and suggest NSS as an alternative standard of care only in healthy patients, particularly when there is a need to preserve renal function.^{1 and 2} Several recent population reviews together with smaller single or multi-institutional studies have showed that the cancer-specific survival is similar in patients undergoing partial or radical nephrectomy for T1b lesions.^{6, 7, 8, 10, 11 and 12} Moreover, NSS for renal masses greater than 4 cm seems to be able to provide additional functional benefits and lower incidence of cardiovascular morbidities in the long-term period.¹³

In these larger lesions, the use of a minimally invasive approach is less adopted. Indeed, laparoscopic PN (LPN) is a technically challenging procedure and it is still often confined in the hand of a few expert surgeons in tertiary centers. In recent years, the widespread diffusion of robotic system has bridged the technical difficulties of LPN leading to a broader choice of minimally invasive approach to larger renal masses by robot-assisted PN (RAPN).^{14, 15 and 16}

To date, no study has compared the perioperative outcome of T1b renal tumors after the 3 currently available surgical options, namely, OPN, LPN, and RAPN. With this purpose, we designed the present multicenter comparative study. Analysis was specifically aimed to intraoperative and perioperative data. The secondary aim of the study was to perform a univariate and multivariable analysis looking for predictive factors of Trifecta achievement.

Methods

Data of 285 patients who had RAPN, LPN, and OPN for cT1b renal tumors were extracted from the Registry of Conservative Renal Surgery database (RECORD Project, 19 Italian centers, January 2009-December 2012) promoted by the “Leading Urological No Profit Foundation Advanced Research” (LUNA) of the Italian Society of Urology¹⁷ and from the preliminary data (January 2013-December 2013) of three high-volume centers, participating in the ongoing RECORD2 project (Florence, Careggi Hospital; Brescia, AO Spedali Civili; Orbassano [Turin] San Giovanni Gonzaga Hospital). High-volume centers were defined as ≥ 50 overall cases of PN per year. Surgeons were all skilled in performing either RAPN, LPN, or OPN. Clinical staging included abdominal computed tomography (CT) and chest CT or X-rays. Magnetic resonance imaging was used in a few patients as an alternative to CT. Bone scans and brain CT were obtained only when indicated by the signs and symptoms. Open procedures were performed using mainly a flank retroperitoneal approach. Tumor excision was done by clamping the renal pedicle or with no clamping, using manual compression of the surrounding renal parenchyma. Opened calyces and bleeding sites were sutured and the parenchymal defect was closed with horizontal interrupted sutures with or without the

application of hemostatic agents (FloSeal, Baxter Healthcare; Tachosil, Nycomed; Tabotamp, Ethicon). Minimally invasive laparoscopic and robotic procedures were performed using either a transperitoneal or a retroperitoneal approach according to surgeon's and center's preferences. Tumor excision was done by warm ischemia or with a clampless procedure. An early unclamping after parenchymal sutures on the tumor bed was adopted when indicated. The parenchymal defect was repaired using the sliding-clip technique. Hemostatic agents were used in most cases before cortical closure.

Data Collection

All the variables recorded were prospectively collected in an online controlled database. Estimated glomerular filtration rate (eGFR) was calculated with the Modification of Diet in Renal Disease equation.¹⁸ As pathological variables, tumor nodes metastasis cancer staging system was assigned according to the 2009 version,¹⁹ histological subtypes according to the World Health Organization classification,²⁰ and nuclear grade according to the Fuhrman grading system.²¹ A positive surgical margin was defined as the presence of cancer cells at the level of the inked parenchymal excision surface. No central pathological slide review was provided. The pathological features were assigned by the uropathologists of each participating center.

The complications up to 3 months after surgery were classified according to the Dindo modification of the Clavien system and to the European Association of Urology standardized quality criteria on reporting PN surgical complications.^{22 and 23} Trifecta outcome was defined as simultaneous achievement of WIT <25 min, absence of complications, and negative surgical margin as suggested by Khalifeh et al.³

The hemoglobin and eGFR at 1 and 3 days after surgery were collected and the differences between preoperative and postoperative values were calculated.

Statistical Analyses

Continuous parametric variables were reported as the mean \pm standard deviation (SD), whereas nonparametric variables were reported as the median and interquartile range (IQR). The Mann-Whitney *U*-test and unpaired Student's *t*-test were used to compare continuous variables, as appropriate. Categorical variables are reported as frequencies and proportions. Pearson's chi-square test was used to compare categorical variables. A univariate and multivariable logistic regression was performed for Trifecta outcome. For all statistical analyses, a two-sided $P < .05$ was considered statistically significant. Analyses were performed using SPSS version 20.0 (SPSS Inc., Chicago, IL).

Results

Overall, 133 OPN, 57 LPN, and 95 RAPN were analyzed. Preoperative data are reported in Table 1. Median (IQR) clinical tumor diameter was 5.0 (4.3-5.5) cm and 63% of tumors were mainly exophytic. The 3 groups had comparable body mass index, preoperative hemoglobin, creatinine, eGFR, tumor clinical diameter, and tumor growth pattern (Table 2). Females were more represented in RAPN group (55.8%) compared with LPN group (26.3%; $P = .01$) (Table 2). Patients undergoing RAPN were significantly younger (mean age of 57.3 years; SD 15.1 years) compared with patients in OPN group (mean age of 62.3 years; SD 13.8 years; $P = .01$) (Table 2). Tumors in the LPN group showed a significantly higher mesorenal location (40.4%) compared with those of OPN group (24.8%; $P = .03$) (Table 2).

Table 1.

Overall preoperative data

Preoperative data (n = 285)		
Gender, n (%)	Male	171 60.0%
	Female	114 40.0%
Age, mean SD		60.3 14.3
BMI, median IQR		25.9 23.1-28.4
ECOG, n (%)	0	219 76.8%
	≥1	66 23.2%
Lesion side, n (%)	Right	159 55.8%
	Left	126 44.2%
Clinical diameter, median IQR		5.0 4.3-5.5
Tumor location, n (%)	Polar superior	95 33.4%
	Mesorenal	85 29.8%
	Polar inferior	105 36.8%
	≥50% Exophytic	180 63.2%
Tumor growth pattern, n (%)	<50% Exophytic	97 34.0%
	Entirely endophytic	8 2.8%
Preoperative Hb, median IQR		14.0 13.0-15.0
Preoperative creatinine, median IQR		1.0 0.8-1.0
Preoperative eGFR, median IQR		86.0 68.6-100.0

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; eGFR, estimated glomerular filtration rate; IQR, interquartile rate; SD, standard deviation.

Table options

Table 2.

Comparison of preoperative data between open (OPN), laparoscopic (LPN), and robot-assisted partial nephrectomy (RAPN)

Preoperative data		OPN (n = 133)		LPN (n = 57)		RAPN (n = 95)		P*	P†	P‡
Gender, n (%)	Male	87	65.4%	42	73.7%	42	44.2%	.26	.01	.38
	Female	46	34.6%	15	26.3%	53	55.8%			
Age, mean SD		62,3	13.8	60.0	13.2	57.3	15.1	0.30	.37	.01
BMI, median IQR		26,0	23.2-29.4	25.6	23.5-28.4	25.8	22.5-27.9	0.97	.58	.41
ECOG, n (%)	0	92	69.2%	43	75.4%	84	88.4%	.38	.26	.04
	≥1	41	30.8%	14	24.6%	11	11.6%			
Lesion side, n (%)	Right	68	51.1%	37	64.9%	54	56.8%	.14	.07	.33

Preoperative data		OPN (n = 133)		LPN (n = 57)		RAPN (n = 95)		<i>P</i> *	<i>P</i> †	<i>P</i> ‡
	Left	65	48.9%	20	35.1%	41	43.2%			
	Clinical diameter, median IQR	5,0	4.5-5.6	5.0	4.3-5.5	5.0	4.1-5.3	0.59	.40	.10
Tumor location, n (%)	Polar superior	53	39.8%	12	21.1%	30	31.6%			
	Mesorenal	33	24.8%	23	40.4%	29	30.5%	.03	.46	.30
	Polar inferior	47	35.3%	22	38.6%	36	37.9%			
Tumor growth pattern, n (%)	≥50% Exophytic	91	68.4%	38	66.7%	51	53.7%			
	<50% Exophytic	36	27.1%	18	31.6%	43	45.3%	.57	.12	.24
	Entirely endophytic	6	4.5%	1	1.8%	1	1.1%			
	Hb preoperative, median IQR	14,0	13.0-15.0	14.0	13.0-15.0	14.0	13.0-15.0	0.94	.88	.96
	Creat preoperative, median IQR	0,9	0.7-1.1	1.0	0.9-1.0	1.0	0.9-1.0	0.20	.33	.45
	eGFR preoperative, median IQR	87,0	66.2-102.8	80,0	69.0-96.1	86,0	69.9-98.0	0.13	.16	.99

Abbreviations as in Table 1.

*

OPN vs LPN.

†

LPN vs RAPN.

‡

RAPN vs OPN.

Table options

A comparison of intra- and postoperative outcomes among open, laparoscopic, and robot-assisted approach is reported in Table 3. The minimally invasive approaches, either pure laparoscopic or robot assisted, were more frequently exclusive of high-volume centers; indeed, 93% of LPN and 100% of RAPN were in those centers with high caseload.

Table 3.

Comparison of intraoperative and postoperative data between OPN, LPN, and RAPN

Intra- and postoperative data	OPN (n = 133)	LPN (n = 57)	RAPN (n = 95)	<i>P</i> *	<i>P</i> †	<i>P</i> ‡
-------------------------------	------------------	-----------------	------------------	------------	------------	------------

Intra- and postoperative data	OPN (n = 133)		LPN (n = 57)		RAPN (n = 95)		P*	P†	P‡
High volume center, n (%)	95	71.4%	53	93.0%	95	100.0%	.01	.01	<.0001
Clampless procedures, n (%)	26	19.5%	19	33.3%	13	13.7%	.04	.004	.25
Ischemia time (min), median IQR	16.0	14.0-20.0	24.0	20.0-29.0	18.0	15.0-24.0	<.0001	<.0001	.004
EBL (cc), median IQR	200	100-300	200	100-200	150	100-200	.46	.04	.01
Operative time (min), median IQR	135	110-170	129	110-150	155	120-196	.33	.001	.002
Intraoperative complications, n (%)	8	6.0%	2	3.5%	1	1.1%	.48	.29	.05
Medical postoperative complications, n (%)	17	12.8%	1	1.8%	2	2.1%	.02	.88	.04
Surgical postoperative complications, n (%)	23	17.3%	8	14.0%	8	8.4%	.58	.27	.04
Surgical Clavien 2, n (%)	13	9.8%	4	7.0%	4	4.2%	.54	.45	.11
Surgical Clavien 3, n (%)	7	5.3%	1	1.8%	1	1.1%	.27	.71	.09
Positive surgical margins, n (%)	9	6.8%	1	1.9%	2	2.5%	.18	.82	.16
Trifecta outcome, n (%)	83	62.4%	36	63.2%	66	69.5%	.92	.42	.27
3rd day delta Hb, median IQR	2.0	1.7-3.0	1.0	0.2-3.0	2.4	1.4-3.0	.003	.01	.69
1st day delta eGFR, median IQR	15.2	0.0-28.5	5.2	0.0-16.7	1.2	0.0-12.6	.02	.22	<.0001
3rd day delta eGFR, median IQR	9.2	0.0-27.6	7.2	0.0-14.0	1.9	0.0-14.6	.45	.66	.12
1st month delta eGFR, median IQR	8.7	0.0-19.5	7.3	0.0-14.0	1.6	0.0-13.0	.59	.21	.12

EBL, estimated blood loss; other abbreviations as in Table 1 and Table 2.

*

OPN vs LPN.

†

LPN vs RAPN.

‡

RAPN vs OPN.

Table options

A clampless procedure was significantly more adopted during LPN (33.3%) than during OPN (19.5%; $P = .04$) and RAPN (13.7%; $P = .004$). Median (IQR) WIT was significantly shorter during OPN (16; 14-20 min) than during LPN (24; 20-29 min) ($P < .0001$) and RAPN (18; 15-24 min) ($P = .004$). In the minimally invasive group, robotic assistance allowed for significantly lower ischemia time in comparison with standard laparoscopy ($P < .0001$).

RAPN group showed significantly lower median (IQR) estimated blood loss (EBL) (150; 100-200 cc) compared with those of OPN group (200; 100-300 cc) ($P = .01$) and LPN group (200; 100-200 cc) ($P = .04$).

Median (IQR) operative time was significantly higher in RAPN group (155; 120-196 min) with respect to OPN (135; 110-170 min) ($P = .002$) and LPN (129; 110-150) ($P = .001$). Intraoperative complication rate was lower in RAPN group (1.1%, 1 vascular injury) in comparison with those of LPN group (3.5%; 2 vascular injuries; $P = .29$) and OPN group (6.0%; 3 vascular injuries, 3 pleural lesions causing pneumothorax, 1 splenic lesion, and 1 rib fracture; $P = .05$).

Medical postoperative complications were significantly higher in OPN group if compared with minimally invasive approaches (12.8%, 1.8%, and 2.1%, OPN, LPN, and RAPN, respectively). Overall surgical postoperative complications were lower in RAPN group compared with OPN (8.4% vs 17.3%, $P = .04$) and to LPN approach without statistical significance (8.4% vs 14%, $P = .27$). Clavien 2 and Clavien 3 complication rates were lower for RAPN (4.2% and 1.1%) than for LPN (7% and 1.8%) and OPN (9.8% and 5.3%), although never reaching statistical significance.

LPN and RAPN showed a lower rate of positive surgical margins (SM) compared with OPN, 1.9%, 2.5%, and 6.8% respectively, although not reaching the statistical significance.

Trifecta was achieved in 62.4%, 63.2%, and 69.5% for OPN, LPN, and RAPN, respectively, with no statistical differences among the groups.

Median (IQR) third postoperative day (POD) hemoglobin drop was significantly lower in LPN (1.0; 0.2-3.0) with respect to OPN (2.0; 1.7-3.0) ($P = .003$) and RAPN (2.4; 1.4-3.0) ($P = .01$) groups. Median (IQR) first POD eGFR drop was higher in OPN (15.2; 0.0-28.5) group with respect to LPN group (5.2; 0.0-16.7) ($P = .02$) and to RAPN group (1.2; 0.0-12.6) ($P < .0001$). No differences among the groups were found when comparing median eGFR drop at the third POD and at 30th POD.

When performing univariate analysis (Table 4), none of the approaches was predictive of Trifecta achievement. At multivariable analysis, exophytic tumor growth pattern (odds ratio [OR]: 1.80; 95% confidence interval [CI]: 1.04-3.12; $P = .03$), EBL (OR: 0.997; 95% CI: 0.996-0.999; $P = .001$), and the procedure carried out in high-volume centers (OR: 1.96; 95% CI: 0.94-4.07; $P = .04$) were significant predictive factors for Trifecta achievement.

Table 4.

Univariate and multivariate analysis for Trifecta achievement

All Data	Univariate Analysis for Trifecta	Multivariable Analysis
----------	----------------------------------	------------------------

		Not Achieved		Achieved		P	OR	95% CI	P
Approach, n (%)	OPN	50	37.6%	83	62.4%	.98*			
	LPN	21	36.8%	36	63.2%	.48†			
	RAPN	29	30.5%	66	69.5%	.32‡			
Tumor growth pattern, n (%)	≥50% exophytic	57	31.5%	124	68.5%		1.80	1.04-3.12	.03
	<50% exophytic	43	41.3%	61	58.7%	.09	–	–	–
Tumor location, n (%)	Polar superior	30	31.6%	65	68.4%	.35§			
	Mediorenal	33	38.8%	52	61.2%	.55			
	Polar inferior	37	35.2%	68	64.8%	.65¶			
Clinical diameter, median IQR		5,0	4.3-5.5	5,0	4.3-5.5	.66			
EBL, median IQR		200	120-350	150	100-250	<.0001	.997	0.996-0.999	.001
Clamping pedicle performed, n (%)	No	15	25,9%	43	74,1%	.09			
	Yes	85	37,4%	142	62,6%				
Centers, n (%)	High volume	79	32.5%	164	67.5%	.03	1.96	0.94-4.07	.04
	Low volume	21	50.0%	21	50.0%		–	–	–

CI, confidence interval; other abbreviations as in Table 1 and Table 2.

*

OPN vs LPN.

†

LPN vs RAPN.

‡

RAPN vs OPN.

§

Polar superior vs mediorenal.

||

Mediorenal vs polar inferior.

¶

Polar inferior vs polar superior.

Discussion

Current indications for NSS have been expanded to larger tumors; the trigger to a further expansion of elective indications has been based on the evidence that PN is comparable with radical nephrectomy in oncological outcomes and that renal function is better preserved.^{24 and 25}

Nevertheless, no consensus has been reached yet about the best approach for the treatment of renal tumors greater than 4 cm in size. Available literature states that for T1b tumors, PN should be performed whenever technically feasible and the open approach is still the gold standard.^{1 and 2} LPN is the alternative to OPN in tertiary referral centers, but it is associated with longer WIT and higher complication rates.²⁶ Initial experiences with RAPN show an overall, recurrence-free, and cancer-specific survival in T1b tumors comparable with OPN at a 2-year median follow-up¹⁶ and a trend toward a lower WIT respect to LPN.²⁷ Indeed, the introduction of robotic system, thanks to the advantages of magnified stereoscopic visualization and the articulated instruments, has reduced the technical challenges associated with tumor dissection and renorrhaphy, overcoming the limitations of pure laparoscopic approach.

A few studies focused on the outcomes of RAPN for T1b renal lesions up to date: initial experiences underlined a significant higher WIT in T1b compared with T1a renal tumors, unsupported by significant difference between two groups in terms of functional outcomes and complications.^{28 and 29} None of the published studies is offering a simultaneous comparison among the three surgical approaches to T1b lesions.

Indeed, without a significant difference of preoperative patients and tumor selection between three groups (except for a significantly higher rate of mediorenal lesions in LPN compared with OPN and a statistically but not clinically significant age difference between RAPN and OPN), Trifecta was achieved in 69.5%, 63.2%, and 62.4% of RAPN, LPN, and OPN. The robotic approach was able to significantly reduce WIT in comparison with the pure laparoscopic approach and to significantly reduce intraoperative and postoperative complications in comparison with the standard open approach with a similar positive SM rate in comparison with LPN but lower than OPN although not reaching the statistical significance.

The most possible explanations of reduced complications in robotic approach are attributable to the elevated experience of robotic surgeons that were not in their learning phase (also clear by the fact that we are analyzing cT1b tumors), and to the benefits of minimally invasive surgery in addition to the improved dexterity and vision of robotic system that makes open surgery actions replicable with a robotic approach. Furthermore, the reduced PSM rate in LPN and RAPN in comparison with OPN is considered as an important pointer that minimally invasive surgery is feasible and safe in the treatment of clinical T1b renal tumors.

Clampless procedures were significantly higher in minimally invasive approaches; this could be related to the high-definition view along with the increased abdominal pressure related to the pneumoperitoneum that allows a higher control of bleeding during the excision of renal tumor and permit the surgeon to perform clampless procedure with greater peace of mind. Robotic approach presented a significantly lower rate of clampless compared with LPN, probably for the absence of tactile feedback that requires a perfect visual control in a bloodless field.

Indeed, lowest EBLs were registered with RAPN: this difference, although not clinically relevant, was surely due to a precise microdissection of vasculature of renal pedicle and magnified intra-

operative vision that limits bleeding and allows for selective immediate coagulation but also to the significantly lower rate of clampless procedures in the RAPN group.

For the secondary purpose of the study, we performed a univariate and multivariable analyses. The three approaches were again compared concerning the rate of Trifecta achievement.

The trifecta outcome represents a modern standardized tool to evaluate the quality of NSS and to more easily compare different approaches with PN. Trifecta is accomplished if the three key outcomes of negative cancer margin, minimal renal functional decrease expressed as WIT <25 minutes and no surgical complications are simultaneously realized.^{3, 4 and 5}

Intra-operative EBL and volume center were the most important factors in predicting the likelihood of achieving Trifecta, whereas the surgical approach was not a predictor of a positive trifecta at univariate analysis. At multivariable analysis, the same factors together with tumor growth pattern were found to be independent predictors of Trifecta achievement.

The study was not devoid of limitations. Different surgeons were involved and this could potentially influence the results. However, this might have increased the external validity of the data with respect to a single-center or single-surgeon setting.

Another limit is the lack of standardized anatomical information in the RECORD 1 database generated in 2008 before the publication of the available published nephrometric systems. However, the surgical complexity of renal masses was in any case evaluated by the present study according to multiple variables, as tumor location and growth pattern.

Moreover, in centers with minimally invasive expertise, open approach is nowadays reserved to imperative indications and very challenging tumors alone, unsuitable for a minimally invasive approach, thereby leading to a potential worsening of the outcomes of such an approach for tumors over 4 cm. In the present study, the inclusion of centers with different surgical volumes and of centers with no minimally invasive experience might have overcome this bias.

Nevertheless, the very low proportion of cases coming from low volume centers, treated exclusively by open PN, shows how the indication to PN for T1b tumors is reserved to high-volume centers and still needs to be supported to become a standard vs radical nephrectomy. Conversely, the inclusion of tertiary referral centers for LPN might have improved the results of such an approach acting as a possible confounder in comparing LPN with the other approaches.

We recognize that a randomized-controlled trial would be required to draw definitive conclusions about the gold standard approach for PN in T1b renal tumors.

Notwithstanding these limitations, to the best of our knowledge, this paper would represent a unique report with the worship of a simultaneous comparison of outcomes of all different approaches with NSS for clinically T1b renal tumors.

Conclusion

The present study demonstrated that patients with clinically T1b renal tumors suitable for NSS can be safely treated by a minimally invasive approach either by LPN or RAPN in high-volume centers. If available, robotic approach allows for significantly lower WIT and EBL with higher rate of Trifecta achievement compared with LPN.

References

1.
 - 1
 - S.C. Campbell, A.C. Novick, A. Belldegrun, *et al.*
 - Guideline for management of the clinical T1 renal mass
 - J Urol, 182 (2009), pp. 1271–1279
 - [SD-008]
2.
 - 2
 - B. Ljungberg, K. Bensalah, S. Canfield, *et al.*
 - EAU guidelines on renal cell carcinoma: 2014 update
 - Eur Urol, 67 (2015), pp. 913–924
 - [SD-008]
3.
 - 3
 - A. Khalifeh, R. Autorino, S.P. Hillyer, *et al.*
 - Comparative outcomes and assessment of trifecta in 500 robotic and laparoscopic partial nephrectomy cases: a single surgeon experience
 - J Urol, 189 (2013), pp. 1236–1242
 - [SD-008]
4.
 - 4
 - A.J. Hung, J. Cai, M.N. Simmons, *et al.*
 - “Trifecta” in partial nephrectomy
 - J Urol, 189 (2013), pp. 36–42
 - [SD-008]
5.
 - 5
 - F. Porpiglia, R. Bertolo, D. Amparore, *et al.*
 - Margins, ischaemia and complications rate after laparoscopic partial nephrectomy: impact of learning curve and tumour anatomical characteristics
 - BJU Int, 112 (2013), pp. 1125–1132
 - [SD-008]
6.
 - 6
 - G.M. Badalato, M. Kates, J.P. Wisnivesky, *et al.*
 - Survival after partial and radical nephrectomy for the treatment of stage T1bN0M0 renal cell carcinoma (RCC) in the USA: a propensity scoring approach
 - BJU Int, 109 (2012), pp. 1457–1462
 - [SD-008]
7.
 - 7
 - R.E. Mitchell, S.M. Gilbert, A.M. Murphy, *et al.*
 - Partial nephrectomy and radical nephrectomy offer similar cancer outcomes in renal cortical tumors 4 cm or larger
 - Urology, 67 (2006), pp. 260–264
 - [SD-008]
8.
 - 8
 - R.H. Thompson, S. Siddiqui, C.M. Lohse, *et al.*

- Partial versus radical nephrectomy for 4 to 7 cm renal cortical tumors
- J Urol, 182 (2009), pp. 2601–2606
- [SD-008]
- 9.
- 9
- C.J. Weight, B.T. Larson, T. Gao, *et al.*
- Elective partial nephrectomy in patients with clinical T1b renal tumors is associated with improved overall survival
- Urology, 76 (2010), pp. 631–637
- [SD-008]
- 10.
- 10
- M. Crepel, C. Jeldres, P. Perrotte, *et al.*
- Nephron-sparing surgery is equally effective to radical nephrectomy for T1BN0M0 renal cell carcinoma: a population-based assessment
- Urology, 75 (2010), pp. 271–275
- [SD-008]
- 11.
- 11
- C.J. Weight, B.T. Larson, A.F. Fergany, *et al.*
- Nephrectomy induced chronic renal insufficiency is associated with increased risk of cardiovascular death and death from any cause in patients with localized cT1b renal masses
- J Urol, 183 (2010), pp. 1317–1323
- [SD-008]
- 12.
- 12
- A. Antonelli, V. Ficarra, R. Bertini, *et al.*
- Elective partial nephrectomy is equivalent to radical nephrectomy in patients with clinical T1 renal cell carcinoma: results of a retrospective, comparative, multi-institutional study
- BJU Int, 109 (2012), pp. 1013–1018
- [SD-008]
- 13.
- 13
- U. Capitanio, C. Terrone, A. Antonelli, *et al.*
- Nephron-sparing techniques independently decrease the risk of cardiovascular events relative to radical nephrectomy in patients with a T1a-T1b renal mass and normal preoperative renal function
- Eur Urol, 67 (2015), pp. 683–689
- [SD-008]
- 14.
- 14
- A. Minervini, G. Siena, M. Carini
- Robotic-assisted partial nephrectomy: the next gold standard for the treatment of intracapsular renal tumors
- Expert Rev Anticancer Ther, 11 (2011), pp. 1779–1782
- [SD-008]
- 15.
- 15
- M. Borghesi, E. Brunocilla, R. Schiavina, *et al.*

- Robotic partial nephrectomy: a promising treatment option for T1b and complex renal tumors?
- Eur J Surg Oncol, 39 (2013), p. 1167
- [SD-008]
- 16.
- 16
- M. Maddox, S. Mandava, J. Liu, *et al.*
- Robotic partial nephrectomy for clinical stage t1b tumors: intermediate oncologic and functional outcomes
- Clin Genitourin Cancer, 13 (2015), pp. 94–99
- [SD-008]
- 17.
- 17
- R. Schiavina, A. Mari, A. Antonelli, *et al.*
- A snapshot of nephron-sparing surgery in Italy: a prospective, multicenter report on clinical and perioperative outcomes (the RECORd 1 project)
- Eur J Surg Oncol, 41 (2015), pp. 346–352
- [SD-008]
- 18.
- 18
- L.A. Stevens, C.H. Schmid, *et al.*
- A new equation to estimate glomerular filtration rate
- Ann Intern Med, 150 (2009), pp. 604–612 Erratum in: Ann Intern Med. 2011 Sep 20;155(6):408
- [SD-008]
- 19.
- 19
- F.L. Greene, M. Gospodarowicz, C. Wittekend, *et al.*
- American Joint Committee on Cancer (AJCC) Staging Manual
- (7th ed)Springer, Philadelphia, PA (2009)
- [SD-008]
- 20.
- 20
- J.N. Eble, G. Sauter, J.I. Epstein (Eds.), *et al.*, Pathology and Genetics of Tumors of the Urinary System and Male Genital Organs. World Health Organization Classification of Tumors, IARC Press, Lyon, France (2004)
- [SD-008]
- 21.
- 21
- S. Fuhrman, L.C. Lasky, L. Limas
- Prognostic significance of morphologic parameters in renal cell carcinoma
- Am J Surg Pathol, 6 (1982), pp. 655–663
- [SD-008]
- 22.
- 22
- D. Mitropoulos, W. Artibani, C.S. Biyani, *et al.*
- Quality assessment of partial nephrectomy complications reporting using EAU standardised quality criteria
- Eur Urol, 66 (2014), pp. 522–526
- [SD-008]
- 23.

- 23
- D. Dindo, N. Demartines, P.A. Clavien
- Classification of surgical complications: a new proposal with evaluation in a cohort of 6,336 patients and results of a survey
- *Ann Surg*, 240 (2002), pp. 205–213
- [SD-008]
- 24.
- 24
- A.F. Fergany, K.S. Hafez, A.C. Novick
- Long-term results of nephron sparing surgery for localized renal cell carcinoma: 10-year followup
- *J Urol*, 163 (2000), pp. 442–445
- [SD-008]
- 25.
- 25
- C.J. Weight, B.T. Larson, A.F. Fergany
- Nephrectomy induced chronic renal insufficiency is associated with increased risk of cardiovascular death and death from any cause in patients with localized cT1b renal masses
- *J Urol*, 183 (2010), pp. 1317–1323
- [SD-008]
- 26.
- 26
- A. Volpe, D. Amparore, A. Mottrie
- Treatment outcomes of partial nephrectomy for T1b tumours
- *Curr Opin Urol*, 23 (2013), pp. 403–410 Review
- [SD-008]
- 27.
- 27
- O.M. Aboumarzouk, R.J. Stein, R. Eyraud, *et al.*
- Robotic versus laparoscopic partial nephrectomy: a systematic review and meta-analysis
- *Eur Urol*, 62 (2012), pp. 1023–1033
- [SD-008]
- 28.
- 28
- F. Petros, S. Sukumar, G.P. Haber, *et al.*
- Multi-institutional analysis of robot-assisted partial nephrectomy for renal tumors >4 cm versus ≤4 cm in 445 consecutive patients
- *J Endourol*, 26 (2012), pp. 642–646
- [SD-008]
- 29.
- 29
- M.N. Patel, L.S. Krane, A. Bhandari, *et al.*
- Robotic partial nephrectomy for renal tumors larger than 4 cm
- *Eur Urol*, 57 (2010), pp. 310–316