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ORIGINAL ARTICLE

Robotic partial nephrectomy *versus* radical nephrectomy in elderly patients with large renal masses

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ABSTRACT

BACKGROUND: Recent evidence suggests that the "oldest old" patients might benefit of partial nephrectomy (PN), but decision-making for this subset of patients is still controversial. Aim of this study is to compare outcomes of robotic partial (RPN) or radical nephrectomy (RRN) for large renal masses in patients older than 65 years.

METHODS: We identified 417≥65 years old patients who underwent RRN or RPN for cT1b or ≥cT2 renal mass at 17 high volume centers. Propensity score match analysis was performed adjusting for age, ASA≥3, pre-operative eGFR, and clinical tumor size. Predictors of complications, functional and oncological outcomes were evaluated in multivariable logistic and Cox regression models.

RESULTS: After propensity score analysis, 73 patients in the RPN group were matched with 74 in the RRN group. R.E.N.A.L. Score (9.6±1.7 *vs.* 8.6±1.7; P<0.001), and high complexity (56 *vs.* 15%; P=0.001) were higher in the RRN. Estimated blood loss was higher in the RPN group (200 *vs.* 100 mL; P<0.001). RPN showed higher rate of overall complications (38 *vs.* 23%; P=0.05), but not major complications (P=0.678). At last follow-up, RPN group showed better

functional outcomes both in eGFR (55.4±22.6 *vs.* 45.7±15.7 mL/min; P=0.016) and lower eGFR variation (9.7 *vs.* 23.0 mL/min; P<0.001). The procedure type was not associated with recurrence free survival (RFS) (HR: 0.47; P=0.152) and overall mortality (OM) (0.22; P=0.084).
CONCLUSIONS: RPN in elderly patients with large renal masses provides acceptable surgical, and oncological outcomes allowing better functional preservation relative to RRN. The decision to undergo RPN in this subset of patients should be tailored on a case by case basis.

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KEY WORDS: Nephrectomy; Aged; Patient outcome assessment.

Current urological guidelines recommend partial nephrectomy (PN) as the elective treatment for cT1a renal masses, whereas radical nephrectomy (RN) remains the primary option for cT1b and ≥cT2 tumors.[1, 2] However, PN for large renal masses has begun to be considered a valid and safe treatment option in terms of oncological control, and improved functional outcomes also for larger renal masses.[3] The widespread adoption of robotic surgery and its well-known technical advantages in terms of visualization and handling of the anatomical structures favored the use of robot-assisted PN (RPN) for large renal masses as well.[4, 5] In addition, cardiovascular,[6] and oncological outcomes[7] indicate that PN could also be suitable for elderly patients, who are usually more likely to be elected to RN.[8, 9] Furthermore, recent evidence suggests that the "oldest old" patients might benefit of PN in terms of surgical functional outcomes, and oncological safety.[10-13] However, the rate of elderly patients who underwent PN for large renal mass (cT1b or ≥cT2) in these studies was underrepresented. Moreover, available evidence on robotic radical nephrectomy (RRN) in elderly patients is poor and scarce and without adequate comparison to RPN.

Therefore, the aim of this study was to assess the feasibility and safety of RPN in a large cohort of patients aged ≥65 with large renal masses and to compare the perioperative, functional, and intermediate-term oncological outcomes of RPN *vs.* RRN in this subset of patients, for whom decision-making is still controversial.

Materials and methods

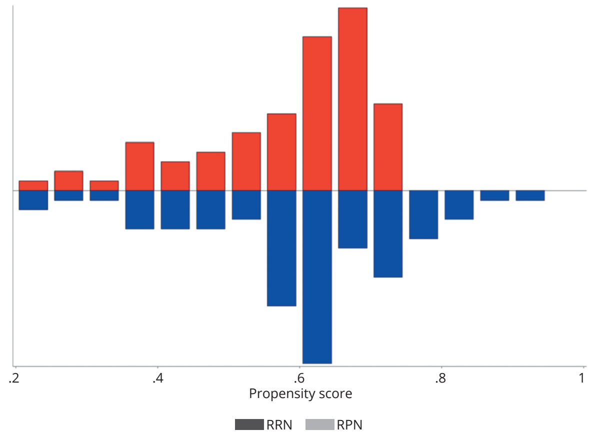
Institutional review board approval and data sharing was obtained at each center involved. All data for the present study were retrieved from a multi-institutional multinational database. Overall, 417 patients 65 years or older who underwent RRN or RPN for cT1b or ≥cT2 renal mass were included.

Baseline patient characteristics (age at the surgery, gender, body mass index [BMI], ASA Score ≥3, diabetes, hypertension, chronic kidney disease ≥class III, preoperative Hb, and estimated glomerular filtration rate [eGFR], and solitary kindey status), clinical staging (tumor size, R.E.N.A.L. Score [continuous and categorical], cT, cN+, cM+), surgical outcomes (transperitoneal approach, operative time [OT], estimated blood loss [EBL], intraoperative transfusions, complications [intraoperative, overall, ≤30 days, major according to Clavien-Dindo classification ≥3], length of stay [LoS], re-admission rate within 30 days, and Hb at discharge), pathological outcomes (tumor size, benign histology, pT, pN+, Fuhrman grade ≥3, positive surgical margins [PSM]), functional outcomes (eGFR and ΔeGFR at discharge, 6, 12, and last follow-up) recurrence free survival (RFS) and overall survival (OS) were assessed.

Statistical analysis

In order to account for any potential baseline differences among the two groups, adjustment was performed using a 1:1 nearest-neighbor propensity score-matching.[14]

Propensity scores were computed using a logistic regression model to account for all measurable potential confounders. The quality of the matching was assessed through the *pstest* and *psgraph* commands. An acceptable matching quality was achieved: before matching B=94.6%, after matching B=22% (Figure 1).



Variable	Unmatched Matched	Mean Treated	Mean Control	%bias	%reduct |bias|	t-test t	t-test p>|t|	V(T)/ V(C)
Ageatsurgery	U	72.372	72.916	-9.7		-0.76	0.445	0.73*
	M	73.129	72.336	14.1	-45.8	0.83	0.406	1.03
1.ASAscore2031	U	.47222	.47126	0.2		0.01	0.988	.
	M	.51351	.47297	8.1	-4132.4	0.49	0.625	.
PreopeGFR	U	67.098	64.484	12.9		0.95	0.342	1.55*
	M	65.913	65.888	0.1	99.1	0.01	0.994	1.78*
ClinicalTumorSizemm	U	65.056	82.632	-91.1		-6.66	0.000	1.76*
	M	82.784	80.811	10.2	88.8	0.77	0.444	0.78

* if variance ratio outside [0.75; 1.34] for U and [0.63; 1.59] for M

Sample	Ps R2	LR chi2	p>chi2	MeanBias	MedBias	B	R	%Var
Unmatched	0.126	42.54	0.000	28.5	11.3	94.6*	1.66	100
Matched	0.009	1.82	0.770	8.1	9.2	22.0	0.73	33

* if B>25%, R outside [0.5; 2]

Figure 1.—Propensity score matching quality.

Statistical analysis was conducted according to guidelines[15] and consisted in three steps. First, Shapiro-Wilk Test was used to establish the distribution of the data. Median (interquartile range [IQR]) was used to report not-parametric data, while mean ± standard deviation (SD) was adopted for parametric data. Proportions were used to report categorical data. To compare the differences in the distribution of continuous and categorical variables between cases treated with RPN and RRN, Mann-Whitney U-test and Fisher's exact were used, respectively. When continuous variables showed parametric distribution, Student's *t*-test was used.

Three separate sets of multivariable logistic and Cox regression models were fitted to evaluate the effect of the type of procedure (RPN *vs.* RRN) on overall complications, eGFR decrease ≥25% (at discharge, 6 and 12 months, and at last follow-up), and RFS and OS. In multivariable models testing for overall complication, adjustment variables consisted of age, ASA≥ 3, R.E.N.A.L. Score, type of procedure (RPN *vs.* RRN), intraoperative transfusion, and intraoperative complications. In multivariable models testing for eGFR decrease ≥25%, adjustment variables were age, ASA≥3, preoperative eGFR, R.E.N.A.L. Score, and type of procedure (RPN *vs.* RRN). In multivariable models testing for recurrence and survival, adjustment variables consisted of R.E.N.A.L. Score and type of procedure (RPN *vs.* RRN). All statistical tests were performed with Stata® 15.0 (StataCorp 2017. Stata Statistical Software: release 15. StataCorp LLC, College Station, TX, USA), and statistical significance was set at P≤0.05.

Results

Baseline characteristics of study cohort before matching

Before matching 143 and 273 patients were found in the RRN and RPN, respectively. The baseline Hb level was higher in the RPN group: 13.9 (12.5-15.1) *vs.* 12.8 (11.7-14.0) g/dL; P<0.001. The RPN group demonstrated smaller tumor size (7.0 *vs.* 8.1 cm; P<0.001), and lower R.E.N.A.L. Score (8.0 *vs.* 10.0; P<0.001) and fewer high complexity masses (30 *vs.* 58%; P<0.001). Patients undergoing RRN had a higher rate of clinically advanced disease (cT≥ 3: 13 *vs.* 9%; P<0.001-cN+ 8 *vs.* 1%; P=0.004-cM+ 19 *vs.* 3%; P<0.001).

Baseline characteristics of study cohort after matching

After propensity score analysis 73 patients in the RPN group were matched with 74 in the RRN one. No statistically significant difference was found in terms of baseline features and tumor dimensions between RPN and RRN groups (P=0.685). However, the R.E.N.A.L. Score (9.6±1.7 *vs.* 8.6±1.7; P<0.001), and proportion of high-complexity tumors (56 *vs.* 15%; P=0.001) were higher in the RRN group compared to RPN.

TABLE I.—*Patients' baseline features and outcomes.*

	Before matching			After matching		
Variables[ƒ]	RRN	RPN	P value	RRN	RPN	P value
Number of patients	143	273		74	73	
Baseline features						
Age (years)	72.0 (68.0-77.0)	72.0 (68.0-76.0)	0.308	71.3 (67.7-77.0)	73.0 (68.0-77.0)	0.388
Gender (male)	95/143 (66%)	195/273 (71%)	0.313	50/74 (67%)	50/73 (68%)	1.000
BMI (kg/m²)	27.7 (24.5-30.2)	26.9 (24.6-30.0)	0.350	27.8 (24.8-31.0)	26.3 (24.3-30.3)	0.284
ASA ≥3	63/114 (55%)	107/226 (47%)	0.135	35/74 (47%)	38/73 (52%)	0.622
Diabetes	38/142 (27%)	63/242 (26%)	0.905	22/73 (30%)	24/69 (35%)	0.594
Hypertension	85/142 (60%)	126/242 (52%)	0.167	43/73 (59%)	34/69 (49%)	0.312
CKD≥III	16/141 (11%)	41/223 (18%)	0.077	11/72 (15%)	16/69 (23%)	0.286
Hb at baseline (g/dL)	12.8 (11.7-14.0)	13.9 (12.5-15.1)	<0.001	13.0 (12.1-14.5)	13.6 (12.5-14.6)	0.111
eGFR at baseline (mL/min/1.73m²) [‡]	64.5±20.2	67.4±22.0	0.216	65.8±17.4	66.1±23.3	0.939
Solitary kidney	1/121 (1%)	12/235 (5%)	0.069	1/74 (1%)	5/73 (7%)	0.116
Clinical tumor staging						
Tumor size (cm)	8.1 (7.2-9.8)	7.0 (5.0-8.0)	<0.001	8.0 (7.1-9.0)	8.0 (7.3-8.6)	0.685
R.E.N.A.L. (continuous)	10.0 (9.0-11.0)	8.0 (7.0-10.0)	<0.001	9.6±1.7[‡]	8.6±1.7[‡]	<0.001
R.E.N.A.L. (complexity)			<0.001			0.001
Low (4-6)	4/122 (3%)	59/245 (24%)		3/68 (4%)	10/73 (14%)	
Intermediate (7-9)	47/122 (39%)	113/245 (46%)		27/68 (40%)	37/73 (51%)	
High (10-12)	71/122 (58%)	73/245 (30%)		38/68 (56%)	11/73 (15%)	
cT			<0.001			0.222
1b	15/135 (11%)	143/272 (53%)		6/66 (9%)	10/73 (14%)	
2a	74/135 (55%)	88/272 (32%)		41/66 (62%)	46/73 (63%)	
2b	26/135 (19%)	16/272 (6%)		5/66 (8%)	9/73 (12%)	
3a	17/135 (13%)	25/272 (9%)		12/66 (18%)	8/73 (11%)	
3b	2/135 (1%)	-		2/66 (3%)	-	
4	1/135 (1%)	-		-	-	
cN+	12/143 (8%)	5/248 (1%)	0.004	5/74 (9%)	2/71 (3%)	0.442
cM+	27/143 (19%)	7/264 (3%)	<0.001	10/74 (13%)	3/73 (4%)	0.078
Surgical outcomes						
Transperitoneal	119/123 (97%)	215/262 (82%)	<0.001	69/70 (98%)	54/72 (75%)	<0.001
OT (min)	174.0 (136.0-225.0)	160.0 (120.0-224.0)	0.049	160.0 (120.0-210.0)	158.0 (115.0-240.0)	0.872
EBL (mL)	100.0 (50.0-200.0)	150.0 (100.0-300.0)	<0.001	100 (50.0-150.0)	200.0 (100.0-475.0)	<0.001
Intraoperative transfusions	6/143 (4%)	15/255 (6%)	0.614	1/74 (1%)	5/72 (7%)	0.114
Intraoperative complications	10/100 (10%)	18/242 (7%)	0.277	3/67 (4%)	8/72 (11%)	0.211
Overall complications	26/125 (20%)	58/243 (24%)	0.600	17/74 (23%)	28/73 (38%)	0.050
Major complications[†]	4/19 (21%)	9/47 (19%)	1.000	3/13 (23%)	4/24 (16%)	0.678
Length of stay (days)	3.0 (2.0-4.0)	4.0 (3.0-6.0)	<0.001	3.0 (2.0-5.5)	5.0 (4.0-7.0)	<0.001
Re-admission 30 days	7/107 (6%)	6/178 (3%)	0.227	4/66 (6%)	3/58 (5%)	1.000
Hb at discharge (g/dL)	11.4 (10.1-12.4)	10.9 (10.0-12.5)	0.470	11.5±1.5[‡]	10.5±1.4[‡]	<0.001
Pathological outcomes						
Tumor size (cm)	8.0 (6.5-9.9)	6.0 (4.8-7.8)	<0.001	7.6±2.3[‡]	7.2±1.9[‡]	0.231
Benign tumor	5/143 (3%)	50/299 (17%)	0.044	5/74 (7%)	11/73 (15%)	0.120
pT≥3	72/143 (50%)	72/273 (26%)	<0.001	40/74 (54%)	23/73 (31%)	0.008
pN+	8/140 (6%)	-	<0.001	4/72 (5%)	-	<0.001
Fuhrman grade ≥3	70/124 (56%)	73/191 (38%)	0.001	32/64 (50%)	30/55 (54%)	0.046
PSM	11/142 (7%)	18/281 (6%)	0.539	10/70 (14%)	7/73 (9%)	0.445
Functional outcomes						
eGFR at discharge (mL/min/1.73m²)	46.0 (37.0-56.9)	60.9 (41.6-71.7)	<0.001	46.0 (37.5-58.6)	57.8 (38.9-70.3)	0.023
ΔeGFR at discharge (mL/min/1.73m²)	12.5 (5.6-28.0)	10.1 (1.29-20.0)	0.027	15.2 (6.0-29.3)	10.9 (1.0-23.0)	0.084
eGFR at 6 months (mL/min/1.73m²)	46.0 (39.0-52.5)	52.1 (41.0-65.7)	0.050	46.0 (39.0-55.7)	51.9 (41.1-66.4)	0.201
ΔeGFR at 6 months (mL/min/1.73m²)	19.0 (10.0-28.0)	10.9 (3.9-20.7)	0.006	19.0 (10.0-29.0)	11.5 (3.3-19.8)	0.032
eGFR at 12 months (mL/min/1.73m²)	45.4 (42.0-58.7)	57.8 (39.9-70.6)	0.023	46.2 (42.0-59.0)	51.9 (34.0-66.4)	0.713

(To be continued)

TABLE I.—*Patients' baseline features and outcomes (continues).*

	Before matching			After matching		
Variables∫	RRN	RPN	P value	RRN	RPN	P value
ΔeGFR at 12 months (mL/min/1.73m²)	16.0 (6.7-27.0)	8.0 (1.2- 10.1)	0.203	16.0 (8.0-27.0)	12.4 (2.6-20.5)	0.262
eGFR at last follow-up (mL/min/1.73m²)	46.0 (37.0-55.0)	61.0 (42.6-75.0)	<0.001	45.7±15.7‡	55.4±22.6‡	0.016
ΔeGFR at last follow-up (mL/min/1.73m²)	22.0 (11.0-29.7)	8.0 (1.2-18.1)	<0.001	23.0 (11.0-31.0)	9.7 (0.7-19.9)	<0.001
Follow-up length (months)	14.5 (6.6-33.8)	22.0 (6.0-42.0)	0.139	12.0 (8.0-27.0)	30.0 (12.0-43.0)	<0.001
eGFR≤45mL/ min/1.73m² at 6 months	30/61 (49%)	30/86 (35%)	0.059	25/51 (49%)	14/37 (38%)	0.385
eGFR≤45mL/ min/1.73m² at last follow-up	41/83 (49%)	48/167 (29%)	0.001	24/46 (50%)	20/55 (36%)	0.225

RRN: robotic radical nephrectomy; RPN: robotic partial nephrectomy; BMI: Body Mass Index; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; OT: operative time; EBL: estimated blood loss; PSM: positive surgical margins.
†Clavien ≥3; ‡mean±standard deviation (SD); ∫median (interquartile range [IQR]), n/N (%).

Surgical outcomes

Regarding surgical outcomes, the transperitoneal approach was preferred with greater prevalence among the RRN group (98 *vs.* 75%; P<0.001). EBL was higher in the RPN group (200.0 [100.0-475.0] mL *vs.* 100 [50.0-150.0] mL; P<0.001), but no difference regarding intraoperative transfusions were observed (P=0.114). Patients undergoing RPN had a higher rate of overall complications (38 *vs.* 23%; P=0.05), but there was no difference between groups for major complications (P=0.678). RPN patients had longer LoS (3.0 *vs.* 5.0 days; P<0.001) (Table I).

In multivariable logistic regression analysis, the type of the procedure did not reach the independent predictor status (OR: 2.22; 95% CI: 0.95, 5.19; P=0.064; Table II).

Histopathological and functional outcomes

The RRN group was found to have more advanced disease as evidenced by a higher rate of pT≥3 (54% *vs.* 31%; P=0.008). The RPN group demonstrated a higher eGFR at discharge [57.8 (38.9-70.3) *vs.* 46.0 (37.5-58.6) mL/min; P=0.023]. At 6 months, eGFR variation was lower in the RPN group [11.5 (3.3-19.8) *vs.* 19.0 (10.0-29.0) mL/min; P=0.032]. At last follow-up, the RPN group maintained a higher eGFR (55.4±22.6 *vs.* 45.7±15.7 mL/min; P=0.016) and lower eGFR variation (9.7 [0.7-19.9] *vs.* 23.0 [11.0-31.0] mL/min; P<0.001). Median follow-up was 19.5 (IQR: 8-40.5) months (Table I, Figure 2). On multivariable logistic regression analysis, RPN reached the independent predictor status for eGFR decrease ≥25% at discharge (OR:

TABLE II.—*Logistic regression of predictors of overall complications.*

	Before matching						After matching					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
Variables	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
Age	0.96	0.92, 1.00	0.107	0.95	0.89, 1.00	0.086	0.97	0.91, 1.03	0.343	0.95	0.88, 1.01	0.155
ASA≥3	2.43	1.41, 4.18	0.001	3.44	1.83, 6.46	<0.001	2.74	1.31, 5.71	0.007	3.65	1.55, 8.59	0.003
R.E.N.A.L. Score	1.07	0.94, 1.22	0.263	1.07	0.91, 1.26	0.352	1.00	0.81, 1.23	0.979	1.00	0.95, 5.19	0.978
Type of procedure												
RRN	Ref			Ref			Ref			Ref		
RPN	1.19	0.70, 2.01	0.507	1.43	0.70, 2.91	0.316	2.08	1.01, 4.27	0.045	2.22	0.95, 5.19	0.064
Intraoperative transfusions	1.31	0.45, 3.80	0.615	0.64	0.14, 2.83	0.560	1.16	0.20, 6.61	0.862	0.56	0.78, 4.02	0.566
Intraoperative complications	1.62	0.63, 4.15	0.310	0.87	0.23, 3.25	0.897	1.40	0.38, 5.08	0.604	0.97	0.23, 4.06	0.975

RRN: robotic radical nephrectomy; RPN: robotic partial nephrectomy; OR: odds ratio; CI: Confidence Interval.

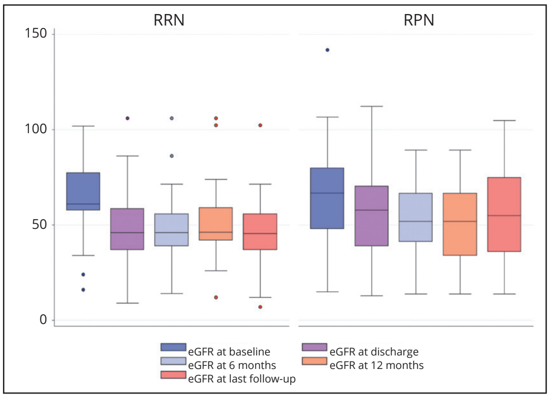


Figure 2.—eGFR values time distribution.

0.33; 95% CI: 0.15, 0.73; P=0.007), at 6 months (OR: 0.23; 95% CI: 0.08, 0.67; P=0.007), and at last follow-up (OR: 0.29; 95% CI: 0.12, 0.72; P=0.008; Table III).

Oncologic outcomes

Using multivariable Cox regression analysis, the type of the procedure was not associated with RFS (HR: 0.47; 95% CI: 0.17, 1.31; P=0.152; Table IV) and OM (0.22; 95% CI: 0.04, 1.21; P=0.084; Table IV). R.E.N.A.L. Score was found to be associated with shorter RFS (HR: 1.40; 95% CI: 1.02, 1.91; P=0.033; Table IV).

Discussion

To the best of our knowledge this study represents the largest report available to date on elderly patients treated with RPN for large renal masses, and the first one providing a comparison between RPN and RRP in this subset of patients. Our analysis revealed some interesting findings which may contribute to the debate on

TABLE III.—*Logistic regression of predictors of eGFR decrease ≥25%.*

	Before matching						After matching					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
Variables	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
eGFR decrease≥25% at discharge												
Age	1.02	0.95, 1.04	0.931	1.02	0.96, 1.08	0.475	1.03	0.97, 1.09	0.328	1.03	0.96, 1.04	0.391
ASA≥3	0.90	0.54, 1.53	0.720	1.05	0.56, 2.00	0.858	0.81	0.41, 1.62	0.568	1.22	0.54, 2.75	0.625
Preoperative eGFR	1.01	1.00, 1.03	0.003	1.02	1.00, 1.04	0.002	1.02	1.00, 1.04	0.004	1.03	1.01, 1.05	0.004
R.E.N.A.L. Score	1.10	0.96, 1.25	0.159	1.03	0.88, 1.21	0.677	1.03	0.83, 1.23	0.895	0.99	0.79, 1.25	0.998
Type of procedure												
RN	Ref						Ref					
PN	0.42	0.25, 0.70	0.001	0.26	0.14, 0.52	<0.001	0.42	0.20, 0.84	<0.001	0.33	0.15, 0.73	0.007
eGFR decrease≥25% at 6 months												
Age	1.00	0.94, 1.06	0.849	0.99	0.92, 1.06	0.856	1.00	0.93, 1.08	0.819	0.99	0.91, 1.07	0.833
ASA≥3	1.02	0.52, 2.02	0.933	1.33	0.58, 3.04	0.489	0.97	0.41, 2.26	0.953	1.06	0.38, 2.97	0.901
Pre-operative eGFR	1.02	1.00, 1.04	0.007	1.03	1.00, 1.05	0.006	1.01	0.99, 1.04	0.094	1.02	0.99, 1.04	0.110
R.E.N.A.L. Score	0.99	0.83, 1.19	0.966	0.86	0.69, 1.07	0.203	0.98	0.76, 1.25	0.879	0.87	0.64, 1.17	0.367
Type of procedure												
RN	Ref			Ref			Ref			Ref		
PN	0.29	0.15, 0.59	0.001	0.21	0.09, 0.50	<0.001	0.27	0.11, 0.67	0.005	0.23	0.08, 0.67	0.007
eGFR decrease≥25% at 12 months												
Age	1.10	1.03, 1.19	0.005	1.11	1.02, 1.20	0.013	1.07	0.98, 1.17	0.111	1.06	0.97, 1.17	0.180
ASA≥3	1.29	0.61, 2.70	0.494	1.41	0.57, 3.46	0.447	1.23	0.48, 3.14	0.658	1.42	0.47, 4.28	0.526
Pre-operative eGFR	1.01	0.99, 1.03	0.052	1.01	0.99, 1.04	0.095	1.01	0.99, 1.04	0.199	1.01	0.99, 1.04	0.281
R.E.N.A.L. Score	0.95	0.78, 1.17	0.684	0.90	0.71, 1.15	0.428	0.83	0.64, 1.09	0.201	0.83	0.61, 1.14	0.263
Type of procedure												
RN	Ref			Ref			Ref			Ref		
PN	0.45	0.21, 0.95	0.038	0.34	0.14, 0.86	0.024	0.77	0.30, 1.99	0.598	0.58	0.19, 1.77	0.344
eGFR decrease≥25% at last follow-up												
Age	1.04	0.99, 1.09	0.073	1.04	0.97, 1.10	0.205	1.02	0.95, 1.10	0.449	1.02	0.95, 1.10	0.477
ASA≥3	0.71	0.40, 1.25	0.241	0.70	0.34, 1.44	0.342	0.51	0.23, 1.14	0.105	0.64	0.24, 1.69	0.371
Pre-operative eGFR	1.00	0.99, 1.02	0.188	1.00	0.99, 1.02	0.341	1.01	0.99, 1.03	0.240	1.00	0.98, 1.03	0.430
R.E.N.A.L. Score	1.21	1.04, 1.40	0.013	1.03	0.85, 1.24	0.747	0.97	0.77, 1.24	0.859	0.91	0.70, 1.18	0.495
Type of procedure												
RN	Ref			Ref			Ref			Ref		
PN	0.16	0.09, 0.29	<0.001	0.17	0.08, 0.36	<0.001	0.28	0.12, 0.64	0.003	0.29	0.12, 0.72	0.008

eGFR: estimated glomerular filtration rate; RN: radical nephrectomy; PN: partial nephrectomy; OR: odds ratio; CI: Confidence Interval.

TABLE IV.—*Cox regression of predictors of RFS and OM.*

	Recurrence free survival			Overall survival		
Variables	HR	95% CI	P value	HR	95% CI	P value
R.E.N.A.L. Score	1.40	1.02, 1.91	0.033	1.35	0.85, 2.14	0.194
Type of procedure						
RN	Ref			Ref		
PN	0.47	0.17, 1.31	0.152	0.22	0.04, 1.21	0.084

RN: radical nephrectomy; PN: partial nephrectomy; HR: hazard ratio; CI: Confidence Interval.

nephron sparing surgery (NSS) for large (cT1b and cT2) tumors.

After propensity score analysis, we found no statistically significant difference in terms of baseline features, even for CKD≥ stage III and solitary kidney. This data mirrors previous literature regarding PN on RN performed for large renal masses. Mir *et al.* described similar findings within a systematic review and meta-analysis of 21 case-control studies on this topic.[3] However, in our analysis we noticed a clinical trend to favor RPN over RRN in patients with CKD≥ stage III (23% *vs.* 15%) or solitary kidney (7% *vs.* 1%). In addition, recent evidence that NSS might provide better cancer specific mortality may warrant consideration for large renal masses even in an elective setting.[6, 16]

Contrary to previous reports, we found no statistically significant difference regarding clinical tumor size; however, RRN was mostly performed for complex tumors. Given the median age of our cohort, one might argue that this could be consequence of the patients age, who are usually managed with RN than PN due to concerns of surgical complications.[8] Nevertheless, NSS for large renal masses is challenging in every subset of patients, and tumor complexity is one of the main factors considered during pre-operative planning. Despite this, NSS for high complexity tumors has shown to be feasible in experienced hands. Indeed, Buffi *et al.* evaluated the outcomes of 255 patients who underwent RPN at tertiary referral centers in a multicenter design study and achieved optimal surgical outcomes in 158 (62%) patients.[17] Their findings were consistent with ours, despite the lack of an elderly population. In fact, even if we found RPN to be associated with higher EBL, the difference with RRN was of only 100 mL which is clinically insignificant. To confirm this data there was no statistically significant difference in terms of intraoperative transfusions.

In our cohort we noticed a higher rate of overall complications in the RPN group, but no difference in major complications. This rate of complications is likely owed to the more complex nature of the RPN procedure during which the risk is increased by the tumor resection and reconstructive phase. Indeed, tumor excision might provoke pelvicalyceal system effraction, and vascular injury, especially during challenging procedures.[18] Our data showed that the only 4 major complications in the RPN group were 3 urine leakage that required ureteral stent placement, and 1 abdominal bleeding which was managed with endovascular embolization. In addition, we found that ASA Score≥3, but no surgical technique, was the only factor associated with the risk of overall complications. Overall, our data suggest that RPN is feasible and potentially safe, but treatment decision between RPN and RRN must be balanced between outcomes, patients comorbidities, and quality of life which is more important than life expectancy itself in elderly patients.[19, 20] In addition, the higher rate of overall complications rate translated into longer LoS in the RPN, another important factor to be considered in elderly patients.[21]

Regarding pathological outcomes, patients undergoing RRN were found to have more advanced disease. This data is consistent with that of a recent report assessing outcomes of RN and PN within the RESURGE Project. In that study the authors assessed 1226 patients older than 75 years and found higher rate of pT≥3 in those cases who underwent RN.[12]Again, Venkatramani *et al.* assessed outcomes of RN and PN for cT1b-cT2 within the National Cancer Database. After propensity score analysis the authors matched

6072 patients per each group showing higher rate of pT≥3 in the RN group (13.1% *vs.* 6.9%; P<0.001).[22] In our data the overall rate of pT≥3 was higher for both groups (RPN 31% *vs.* RRN 54%), but this difference could be explained by the different covariates selection to build the propensity model.

When comparing RPN and RRN, the functional outcomes assessment deserves attention. RPN provided better kidney function compared to RRN, especially at medium and long-term follow-up. Indeed, the advantages of NSS surgery were not immediately obvious, whereas at last follow-up eGFR and eGFR variation were better for the RPN group. Nevertheless, the difference was of only about 10 mL/min and may not be clinically significant, but this could be the case in this subset of patients whose kidney function could be already impaired.[23] Of note, on multivariable analysis RPN showed a protective role regarding eGFR decrease ≥25%. These data mirror literature evidence which largely assessed the functional advantages of nephrons unit preservation. A recent report compared function results of 250 living donors and 118 partial nephrectomy patients. The authors evaluated % eGFR variation at discharge, 1-7 months, and last follow-up, and achieved the conclusion that PN provided immediate better functional outcomes and that should be considered, even at expense of longer ischemia time.[24] If this could be true for small renal masses, it might be different for large and complex ones. Recently, Wu *et al.* conducted a refined analysis of the functional impact of the vascularized parenchymal mass preserved with partial nephrectomy and predictors. The authors identified four possible scenarios (1-4) based upon the percentage of parenchymal mass preserved after PN. The analysis demonstrated that high tumor complexity and dimension were related to suboptimal preservation of nephrons due to the larger resection and reconstruction. This could impair functional recovery despite NSS.[25] Given these findings, our study demonstrated RPN to provide better functional outcomes for large and complex renal masses in the subset of elderly patients, as already underlined in other reports.[11, 12]

Survival outcomes demonstrated RFS to be associated to R.E.N.A.L. Score, whereas surgical procedure (RPN or RRN) was not found to be a predictor. This data corroborates those of previous studies assessing R.E.N.A.L. Score as predictor of malignancy, more advanced pathology, and recurrence. Nagahara *et al.* demonstrated that high R.E.N.A.L. Score is associated with RFS (HR: 9.05; P=0.0019).[26]

Limitations of the study

To the best of our knowledge this is the largest report describing the outcomes of elderly patients after RPN or RRN for large renal masses. This analysis is strengthened by the propensity score design and the sample size. Despite this, it is not devoid of limitations. First, the retrospective nature introduces biases which cannot be avoided. Even if these were limited with the propensity score matched analysis, it presented a bias of 22%. Moreover, the aim to balance the two groups according to surgical technique reduced the numerosity of the two groups. A second important limitation is the absence of others fragility scores to assess patient's performance status and life expectancy. This analysis cannot be generalized to all clinical realities because all the procedures were performed in high volume centers with high proficiency in robotic and renal surgery. Kidney function was evaluated through eGFR which could be misleading because of the compensatory function of the contralateral kidney.[27, 28] Last, but not least, the follow-up period could be too short to evaluate accurately survival outcomes. Moreover, the follow-up length was significantly longer in patients undergoing RRN. As such, our findings on oncological outcomes should be interpreted with caution. Notwithstanding these limitations, this report provides further data regarding the management of large renal masses even in elderly population.

Conclusions

RPN in elderly patients with large renal masses offers acceptable surgical, functional, and oncological outcomes compared to RRN. The decision to undergo RPN in this subset of patients should be tailored on a case by case basis.

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