# Outcomes of Partial and Radical Nephrectomy in Octogenarians — A Multicenter International Study (Resurge)

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**OBJECTIVE** To analyze the outcomes of partial nephrectomy (PN) and radical nephrectomy (RN) in octogenarian patients.

**METHODS** The RESURGE (REnal SUrgery in the Eldely) multi-institutional database was queried to identify patients ≥80 years old who had undergone a PN or RN for a renal tumor. Multivariable binary logistic regression estimated the association between type of surgery and occurrence of complications. Multivariable Cox regression model assessed the association between type of surgery and All-Causes Mortality.

**RESULTS** The study analyzed 585 patients (median age 83 years, IQR 81-84), 364 of whom (62.2%) underwent RN and 221 (37.8%) PN. Patients undergoing RN were older ($P = .0084$), had larger tumor size ($P < .0001$) and higher clinical stage ($P < .001$). At multivariable analysis for complications, the only significant difference was found for lower risk of major postoperative complications for laparoscopic RN compared to open RN (OR: 0.42; $P = .04$). The rate of significant (>25%) decrease of eGFR in PN and RN was 18% versus 59% at 1 month, and 23% versus 65% at 6 months ($P < .0001$). After a median follow-up time of 39 months, 161 patients (31%) died, of whom 105 (20%) due to renal cancer.

**CONCLUSION** In this patient population both RN and PN carry a non-negligible risk of complications. When surgical removal is indicated, PN should be preferred, whenever technically feasible, as it can offer better preservation of renal function, without increasing the risk of complications. Moreover, a minimally invasive approach should be pursued, as it can translate into lower surgical morbidity. UROLOGY 129: 139–145, 2019. © 2019 Elsevier Inc.

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Renal Cell Carcinoma (RCC) has a peak in its incidence between the sixth and seventh decade, but older patients cover up to a third of new diagnoses,[1] and their number is on the rise given prolonged life expectancy. Thus, urologists, oncologists, and geriatricians will be increasingly facing with the complex issue of how to manage RCC in the "very" elderly. Especially in this setting, patients' and tumor's features needs to be considered to assess which management option offers the optimal trade-off between risks and benefits.

Despite general trend is in favor of partial nephrectomy (PN) and minimally invasive approaches,[2] in many centers open radical nephrectomy still represents the preferred surgical way in very elderly subjects.[3] Evidence supporting nephron-sparing and minimally invasive approaches for these subjects remains sparse, and studies adopted liberal definitions of "elderly" (as over 65, 70, or 75 years[4,5]).[6] Only a handful number of small series focused their attention "octogenarians" or "oldest old," as defined by the World Health Organization.[7]

The aim of this study was to provide a comprehensive comparison of surgical, functional, and survival outcomes of PN versus RN in these "very elderly" (octogenarian) patients through the analysis of a multi-institutional international dataset (RESURGE: REnal SURGery in the Elderly).

## MATERIAL AND METHODS

### Study Design

The RESURGE project involves 23 Institutions from Europe, United States, and Asia, with the objective to collect a large dataset on elderly patients undergoing surgery for RCC between 2000 and 2016. A data-sheet was shared and merged, reporting pre-, intra- and postoperative data, functional and survival follow-up information.[8,9] Institutional Review Board approval was obtained by each center.

The present study retrospectively analyzes the patients aged 80 years old or more with complete data. Comorbidities were described by the Charlson-Romano score[10]; Glomerular Filtration Rate was estimated (eGFR) by the chronic kidney disease epidemiology collaboration (CKD-EPI) formula[11]; the staging system was updated to the 2017 edition of the TNM classification[12]; postoperative complications were classified in agreement with the Clavien-Dindo system.[13] The indication to surgery, as well as the type of surgery (PN or RN) and approach were established at each Institution following surgeon's and patient's preferences. Follow-up was conducted according to various schedules at each Institution and incomplete data were retrieved by registries consultation or phone interview. The causes of death were detailed as due to RCC or other reasons.

### Statistical Analysis

Categorical variables were described as numbers and proportions; continuous variables as medians and interquartile range (IQR). Patients submitted to PN versus RN were compared by the Pearson's chi-square test and Kruskal-Wallis h test for categorical and continuous variables, respectively.

Multivariable binary logistic regression estimated the association between the type of surgery (PN or RN) and the occurrence of intra-, overall postoperative and major postoperative complications. Potential confounders (age, gender, BMI, Charlson score−0 vs 1-2 vs ≥3, open vs laparoscopic vs robotic approaches, pathological tumor size, R.E.N.A.L. score, pT−pT1 vs pT2 vs pT > 2, pN−pN0 vs pNx vs pN+, low vs high grading) were initially tested at univariate analysis and only those with a $P$ significance <.1 were included into final multivariable analysis.

Following a similar design, multivariable Cox regression model assessed the association between the type of surgery and All-Causes Mortality (ACM), imputing time intervals as the period in months between surgery and death due to RCC or other causes or the last available control. All statistical analysis was performed with STATA15 (StataCorp LLC, College Station, TX).

## RESULTS

The study analyzed the data of 585 "octogenarian" patients (median age 83 years, IQR 81-84), 364 of whom (62.2%) underwent RN and 221 (37.8%) PN. Patients undergoing RN were older (83.1 vs 82.4 years, $P = .0084$), had lower prevalence of hypertension (58% vs 70%, $P = .005$), higher rate of baseline CKD stage III (47% vs 30%, $P = .038$), larger clinical size (5.9 vs 3.5 cm, $P < .0001$), higher clinical stage ($P < .001$). Baseline eGFR and distribution of Charlson scores were similar between groups. Moreover, pathological tumor size, pathological staging, and grading were more advanced in the RN group (Table 1).

### Perioperative Morbidity

PN had shorter operative time (150 [IQR 118-200] vs 170 [125-220] min; $P = .020$) and similar EBL (200 [100-400] vs 225 [100-400] mL; $P = .1573$), whereas no difference was recorded for complications between the 2 study groups (Table 2).

At multivariable analysis for complications, the only significant difference was found for lower risk of major postoperative complications for laparoscopic RN compared to open RN (OR: 0.42; $P = .04$) (Table 3). A detailed description of complications is summarized in electronic supplementary table 1.

### Functional Outcomes

Starting from similar baseline eGFR (RN median eGFR 60 mL/min, IQR 45-73; PN 60 mL/min, IQR 46-77, $P = .3588$), the observed variations in eGFR after PN and RN were −3 (IQR −13, 0) versus −16 (IQR −26, −8) mL/min and −6 (−14, 0) versus −17 (−27, −8) mL/min, at 1 and 6 months respectively. The respective percentage variations were −3% (IQR −13%, 0%) versus −35% (IQR −42%, −13%) and −6% (IQR −14%, 0%) versus −31% (IQR −42%, −15%) (all $P$ values < .0001). The rate of significant (>25%) decrease of eGFR in PN and RN was 18% versus 59% at 1 month, and 23% versus 65% at 6 months (all $P < .0001$).

### Survival Analysis

After a median follow-up time of 39 months (IQR 12-54), 161 patients (31%) died, 105 (20%) due to renal cancer and 59 (11%) for other causes. At univariate analysis ACM was associated to a Charlson index ≥3 (HR 1.6, $P = .017$), type of surgery (RN referent, HR for PN 0.7, $P = .033$) and a pT stage ≥3 (pT1-2 referent, HR for pT ≥3 1.5, $P = .066$). However, none of these factors reached statistical significance at multivariable analysis (Table 4).

**Table 1.** Baseline comparison between patients who underwent RN and PN

| | RN (364)[a] | PN (221)[a] | *P* Value |
|---|---|---|---|
| **Patients' baseline features** [f] | | | |
| Age (years) | 83.1 ± 2.7 | 82.3 ± 2.0 | **.008** |
| Female gender | 181 (49.7) | 122 (55.2) | .199 |
| BMI (kg/m$^2$) | 25.4 ± 3.8 | 25.7 ± 3.6 | .145 |
| Diabetes | 82 (23.1) | 41 (20.1) | .410 |
| Hypertension | 206 (58.2) | 142 (70.3) | **.005** |
| Preoperative Hb (mg/dL) | 12.3 ± 2 | 12.8 ± 1.9 | **.006** |
| Preoperative eGFR (mL/min) | 58.7 ± 19.7 | 60.4 ± 20.3 | .358 |
| CKD stage III | 55 (47) | 17 (30.4) | **.038** |
| Charlson group categories | | | .652 |
| 0 | 51 (19.6) | 33 (18.5) | |
| 1-2 | 91 (35) | 70 (39.3) | |
| ≥3 | 118 (45.4) | 75 (42.2) | |
| **Preoperative tumor's features** [f] | | | |
| R.E.N.A.L. Score (Complexity) | | | **<.001** |
| 4-6 (Low) | 33 (17.7) | 69 (48.6) | |
| 7-10 (Intermediate) | 120 (64.5) | 69 (48.6) | |
| >10 (high) | 33 (17.8) | 4 (2.8) | |
| Clinical dimension (cm) | 5.9 ± 2.7 | 3.6 ± 1.4 | **<.001** |
| cT stage | | | **<.001** |
| 1 | 108 (29.7) | 171 (77.4) | |
| 2 | 163 (44.8) | 44 (19.9) | |
| 3 | 75 (20.6) | 5 (2.3) | |
| 4 | 18 (4.9) | 1 (0.4) | |
| cN stage | | | **.013** |
| 0 | 280 (90.6) | 186 (97.4) | |
| 1 | 26 (8.4) | 4 (2.1) | |
| 2 | 3 (1) | 1 (0.5) | |

RN, radical nephrectomy; PN, partial nephrectomy; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated Glomerular Filtration Rate; SD, standard deviation.
[f] SD, or no. (%).
[a] Number of patients.

## DISCUSSION

Current guidelines recommend PN over RN in resectable cT1 RCC, as better preservation of renal function protects from cardiovascular events,[14] and, according to more recent evidence, might even decrease cancer-specific mortality.[15] While the debate on which patients are really harmed by RN is ongoing,[16] several studies suggest that PN might be especially advantageous in more comorbid and frailer subjects.[17] However, in clinical practice RN seems to be still preferred to PN in the oldest patients. Population studies on large US datasets indeed show that PN for T1a RCC is done in 68% of 20-44 years subjects,[18] but only 28% in those over 65 years old.[19] These figures suggest that PN is generally disregarded in elderly patients likely because they are considered at higher risk for surgery-related complications. This translates into neglecting the potential advantages related to a better preservation of an already compromised baseline renal function.

The present study gives an insight in a large, multi-institutional cohort of "oldest old" (octogenarian) patients, a population representing probably the contemporary frontier for surgery, being close to the limit of life expectancy in industrialized countries.[7] The analysis of this unique dataset allowed some interesting findings.

First, PN or RN were both adopted as surgical approach at the participating Institutions, and minimally invasive approach was preferred in about 40% of cases. Not surprisingly, RN was preferred for larger (mean tumor size 5.9 cm) and higher stage (70% clinical stage T2-4) tumors, whereas PN was mostly adopted for the so called small renal mass (mean tumor size 3.5 cm and about 80% cT1 stage). Second, both RN and PN carry a non-negligible number of overall and major complications in this patient population. In this respect, our data are consistent with those of literature.[20-22] Nevertheless, our analysis also suggests that, despite being a potential more harmful procedure, PN might not carry a higher risk of complications over RN, and therefore it should not be discouraged solely based on the elderly age. Third, it is confirmed that PN offered a significant higher preservation of renal function keeping these subjects with borderline or impaired baseline function within safety limits with respect to end-stage CKD. Last, we found that despite advanced age, RCC represents a primary cause of death, confirming that elderly patients are often burdened by more aggressive and lethal tumors, as previously reported.[23] ACM was not influenced by the type of surgery but comorbidities and tumor stage, confirming that PN provide equivalent survival as RN, but also indicating that within this age group no survival advantages should be expected.[22]

The available literature on kidney cancer surgery in octogenarian patients remains sparse, with only a handful

**Table 2.** Surgical outcomes

| | Total (n = 585) | RN (n = 364) | PN (n = 221) | *P* Value |
|---|---|---|---|---|
| **Surgical outcomes** [f] | | | | |
| **Surgical technique** | | | | **<.001** |
| Open | 336 (57.5) | 223 (61.3) | 113 (51.1) | |
| Laparoscopic | 177 (30.2) | 135 (37.1) | 42 (19.0) | |
| Robotic | 67 (11.4) | 4 (1.1) | 63 (28.5) | |
| Missing | 5 (0.9) | 2 (0.5) | 3 (1.4) | |
| **Operative time (min)** | - | 178.8 ± 75.8 | 162.6 ± 66.9 | **.020** |
| **EBL (mL)** | - | 352.3 ± 296.7 | 300.2 ± 337.7 | .158 |
| **Intraoperative complications** | 61 (10.4) | 42 (11.5) | 19 (8.6) | .259 |
| **Postoperative complications** | 146 (25.0) | 89 (24.5) | 57 (25.8) | .716 |
| **Major complications** | 32 (5.5) | 21 (5.8) | 11 (5.1) | .690 |
| Open | 25 (4.3) | 18 (8.0) | 7 (6.2) | |
| Laparoscopic | 5 (0.9) | 3 (2.2) | 2 (4.8) | |
| Robotic | 2 (0.3) | 0 (0.0) | 2 (3.2) | |
| **Pathological outcomes** [f] | | | | |
| **Tumor histology** | | | | **<.001** |
| Benign | 42 (7.2) | 13 (3.6) | 29 (13.1) | |
| Malignant | 527 (90.1) | 348 (95.6) | 179 (81.0) | |
| Missing | 16 (2.7) | 3 (0.8) | 13 (5.9) | |
| **pT stage** | | | | **<.001** |
| 1 | 368 (62.9) | 221 (60.7) | 147 (66.5) | |
| 2 | 54 (9.2) | 49 (13.5) | 5 (2.3) | |
| ≥ 3 | 88 (15.0) | 78 (21.4) | 10 (4.5) | |
| Missing | 75 (12.8) | 16 (4.4) | 59 (26.7) | |
| **Grading** | | | | **.003** |
| 1-2 | 307 (52.5) | 185 (50.8) | 123 (55.6) | |
| 3-4 | 205 (35.0) | 149 (40.9) | 56 (25.3) | |
| Missing | 73 (12.5) | 30 (8.3) | 42 (19.0) | |
| **Functional outcomes** [f] | | | | |
| Preoperative eGFR | - | 58.7 ± 19.7 | 60.4 ± 20.3 | **<.001** |
| Post-operative eGFR at 6th months | - | 39.6 ± 12.8 | 51.6 ± 19.2 | **<.001** |
| eGFR variation | - | −17.0 ± 13.9 | −7.6 ± 11.0 | **<.001** |

EBL= Estimated Blood Loss
[f] SD, or no (%).

number of studies specifically focusing on the "oldest old" (Electronic supplementary table 2). Hellenthal et al showed in a large cohort of patients extracted from Surveillance, Epidemiology, and End Results database that PN was less used for elderly patients and cancer mortality similar in 2 matched groups of ≤80 versus ≥80 years old. The latter group had however higher other causes mortality and was 1.31-folds likely to die for any causes and 2.54 times for RCC when submitted to RN.[6] More recently, May et al performed a multicenter analysis comparing mortality of octogenarians with younger patients showing that cancer-specific mortality was related to age and tumor's features and not to the type of surgery.[24] Tang et al retrospectively analyzed a group of 115 patients with a median age of 82 by comparing active surveillance (AS), PN, and RN. No difference in overall survival or disease-specific survival among the 3 management strategies was found on univariable analysis, and multivariable analysis for overall survival found the Charlson comorbidity index as the only factor associated with worse survival. Therefore, the authors concluded that an "active treatment" (either PN or RN) might not provide a survival advantage compared with AS in this group of patients.[25] The feasibility of laparoscopic approaches with acceptable complications rates in these patients was first showed by the studies of Pareek et al[20] and Thomas et al.[21] On the other hand, a multicenter analysis from 5 academic centers in France on 180 octogenarians mostly submitted to open RN (80% of sample) found that morbidity and mortality were significant.[26] In this resp`ect, our analysis shows that a minimally invasive approach for RN should be preferred, as it offers a lower risk (OR = 0.42) of major complications, which especially in this group of patients might have a clinically significant impact.

The present study presents the largest cohort of octogenarians to date reported, and it offers a comprehensive analysis of surgical outcomes. We confirmed that PN and minimally invasive approaches are feasible with lower complications. This is a noteworthy advantage in this subset of patients burdened by risks specifically related to the hospitalization, as falls and fractures, delirium, etc. Moreover, this is the first study investigating changes in renal function in the oldest old showing that PN could avoid or delay end-stage CKD with its detrimental effects in such population.[5] Finally, we confirmed that patient's comorbidity status and tumor's features rather than type of surgery have an impact on survival, probably because the functional advantages that are attributable to PN end up

**Table 3.** Univariate and multivariate analysis of the relationship between confounders and intraoperative, overall postoperative, and major postoperative complications.

| | Intraoperative Complication | | | | | |
|---|---|---|---|---|---|---|
| | Univariate Analysis | | | Multivariate Analysis | | |
| | OR | 95% CI | *P* Value | OR | 95% CI | *P* Value |
| **Type of surgery**[†] | | | | | | |
| RN | Referent | | | | | |
| PN | 0.72 | 0.40-1.27 | .261 | 0.67 | 0.29-1.54 | .357 |
| **Technique**[‡] | | | | | | |
| Open | Referent | | | | | |
| Laparoscopic | 0.51 | 0.26-0.97 | **.043** | 0.50 | 0.23-1.09 | .085 |
| Robotic | 0.20 | 0.04-0.85 | **.03** | 0.28 | 0.06-1.31 | .107 |
| **Tumor features** | | | | | | |
| Clinical size | 1.01 | 1.00-1.02 | **.008** | 0.99 | 0.96-1.01 | .549 |
| R.E.N.A.L. ≥10 | 2.12 | 1.09-4.12 | **.027** | 1.39 | 0.66-2.94 | .380 |
| cT1 | Referent | | | | | |
| cT2 | 1.46 | 0.78-2.73 | .236 | 1.35 | 0.50-3.65 | .552 |
| cT≥3 | 2.73 | 1.38-5.37 | **.004** | 2.34 | 0.41-13.36 | .337 |
| **Overall Postoperative Complications** | | | | | | |
| **Type of surgery**[†] | | | | | | |
| RN | Referent | | | | | |
| PN | 1.07 | 0.73-1.57 | .716 | 1.67 | 0.89-3.15 | .108 |
| **Technique**[‡] | | | | | | |
| Open | Referent | | | | | |
| Laparoscopic | 0.57 | 0.37-0.89 | **.013** | 0.73 | 0.42-1.26 | .270 |
| Robotic | 0.26 | 0.11-0.60 | **.002** | 0.38 | 0.14-1.00 | .052 |
| **Tumor features** | | | | | | |
| Tumor size | 1.01 | 1.00-1.01 | **.004** | 1.01 | 0.99-1.03 | .107 |
| cT1 | Referent | | | | | |
| cT2 | 1.78 | 1.17-2.71 | **.007** | 1.55 | 0.73-3.31 | .247 |
| cT≥3 | 1.81 | 1.07-3.05 | **.009** | 1.03 | 0.26-4.11 | .960 |
| **Postoperative Major Complications** | | | | | | |
| **Type of surgery**[†] | | | | | | |
| RN | Referent | | | | | |
| PN | 0.85 | 0.40-1.81 | .683 | 2.05 | 0.80-5.21 | .131 |
| **Technique**[‡] | | | | | | |
| Open | Referent | | | | | |
| Laparoscopic | 0.36 | 0.13-0.96 | **.042** | 0.42 | 0.15-1.14 | **.04** |
| Robotic | 0.38 | 0.89-1.68 | .206 | 0.44 | 0.09-2.14 | .314 |
| **Tumor features** | | | | | | |
| Tumor size | 1.01 | 1.00-1.02 | **.007** | 1.02 | 0.99-1.04 | .106 |
| cT1 | Referent | | | | | |
| cT2 | 3.25 | 1.31-8.06 | **.011** | 2.49 | 0.80-7.79 | .115 |
| cT≥3 | 3.88 | 1.40-10.73 | **.009** | 1.12 | 0.14-8.40 | .910 |

OR, odds ratio; CI, confidence interval.
[†] Radical Nephrectomy versus Partial Nephrectomy.
[‡] Open versus Laparoscopic versus Robotic.

being diluted in subjects with shorter life expectancy. Nevertheless, octogenarian are patients to whom the best choice treatment still remains a dilemma. General conditions, changed physiology, life expectancy, medications, and patients' expectations make elderly suitable for other kind of treatments. In a significant portion of the aforementioned population, AS represents a valid alternative treatment which is gaining more relevance. Literature evidences demonstrated that on careful selected patients AS gives valuable results. Indeed, in a review on 17 studies

**Table 4.** Comparison between univariate and multivariate analysis of the relationship between type of the surgery and ACM.

| | Univariate Analysis | | | Multivariate Analysis | | |
|---|---|---|---|---|---|---|
| | HR | 95% CI | *P* Value | HR | 95% CI | *P* Value |
| **Charlson ≥ 3** | 1.59 | 1.08-2.34 | **.017** | 1.40 | 0.94-2.09 | .093 |
| **pT ≥ 3** | 1.52 | 0.97-2.38 | **.066** | 1.53 | 0.95-2.45 | .074 |
| **PN**[†] | 0.65 | 0.44-0.96 | **.033** | 0.91 | 0.58-1.43 | .705 |

HR, hazard ratio; CI, confidence interval.
[†] Radical nephrectomy versus partial nephrectomy.

including 36,496 elderly, it was shown that AS presents a low rate of conversion to active treatment with mortality related more to comorbidities rather than RCC.[26] Likewise, less invasive treatment as small renal mass ablation could be considered as an alternative in octogenarian. Among the few studies available, this procedure demonstrated to be safe and feasible without compromising survival outcomes. Moreover, the analysis of postoperative and functional outcomes revealed optimal results making percutaneous ablation an attractive form of treatment.[27]

Our study is not devoid of limitations. The retrospective design carries inherent biases related to data collection and selection bias for the type of surgery. Such a bias has been widely debated into the literature, and only a randomized trial could account for it. Moreover, the fact that participating Institutions are academic and/or referral centers, which limits the reproducibility of these findings in other types of hospital settings. In addition, given the multicenter nature of the study, there is an intrinsic heterogeneity in surgical technique and expertise among the different institutions (and surgeons) that is difficult to account for, and this should be taken into account when interpreting our study findings. The lack of control groups for AS and tumor ablation can be also regarded as an additional limitation, as these are 2 safe and effective management options in this patients population.[26,27] Moreover, the median study follow-up was just over 3 years, which in general might not be considered fully adequate when studying a population with kidney cancer. However, given the advanced age of these patients (and related limited life expectancy), we believe it is still meaningful to look at this time frame. Last, the lack of validated tools to assess frailty that should become mandatory in future studies in this subset of patients.[28]

## CONCLUSION

The management of renal mass in the octogenarian patient represents a challenging scenario. This multicenter analysis, based on "real life" data, allows to get some useful information that can be used for patient counseling and surgical decision-making. One should be aware that in this patient population both RN and PN can carry a non-negligible risk of complications, and therefore they should be reserved for larger tumors where more conservative approaches (AS; ablation) are suboptimal. When surgical removal is indicated, PN should be preferred over RN, whenever technically feasible, as it can offer better preservation of renal function, without increasing the risk of complications. Moreover, a minimally invasive approach should be pursued in this very frail population, as it can potentially translate into lower surgical morbidity.

## SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urology.2019.03.009.

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