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Minimally invasive nephron-sparing treatments for T1 renal cell cancer in patients over 75 years: a comparison of outcomes after robot-assisted partial nephrectomy and percutaneous ablation

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Abstract

Purpose To compare the oncological and perioperative outcomes of robot-assisted partial nephrectomy (RPN) and percutaneous thermal ablation (PTA) for treatment of T1 renal cell cancer (RCC) in patients older than 75 years.

Materials and methods Retrospective national multicenter study included all patients older than 75 years treated for a T1 RCC by RPN or PTA between January 2010 and January 2021. Patients' characteristics, tumor data, and perioperative and oncological outcomes were compared.

Results A total of 205 patients for 209 procedures (143 RPN and 66 PTA) were included. In the PTA group, patients were older (80.4 ± 3.7 vs. 79 ± 3.7 years ($p = 0.01$)); frailer (ASA score (2.43 ± 0.6 vs. 2.17 ± 0.6 ($p < 0.01$)); and more frequently had a history of kidney surgery (16.7% [11/66] vs. 5.6% [8/143] ($p = 0.01$)) than in the RPN group. Tumors were larger in the RPN group (2.7 ± 0.7 vs. 3.2 ± 0.9 cm ($p < 0.01$)). Operation time, length of hospital stay, and increase of creatinine serum level were higher in RPN (respectively 92.1 ± 42.7 vs. 150.7 ± 61.3 min ($p < 0.01$); 1.7 ± 1.4 vs. 4.2 ± 3.4 days ($p < 0.01$); 1.9 ± 19.3% vs. 10.1 ± 23.7 ($p = 0.03$)). Disease-free survival and time to progression were similar (respectively, HR 2.2; 95% CI 0.88–5.5; $p = 0.09$; HR 2.1; 95% CI 0.86–5.2; $p = 0.1$). Overall survival was shorter for PTA that disappeared after Cox adjusting model (HR 3.3; 95% CI 0.87–12.72; $p = 0.08$).

Conclusion Similar oncological outcomes are observed after PTA and RPN for T1 RCC in elderly patients.

Clinical relevance statement Robot-assisted partial nephrectomy and percutaneous thermal ablation have similar oncological outcomes for T1a kidney cancer in patients over 75 years; however, operative time, decrease in renal function, and length of hospital stay were lower with ablation.

Key Points

- *After adjusting model for age and ASA score, similar oncological outcomes are observed after percutaneous thermal ablation and robot-assisted partial nephrectomy for T1 renal cell cancer in elderly patients.*
- *Operation time, length of hospital stay, and increase of creatinine serum level were higher in the robot-assisted partial nephrectomy group.*

Keywords Aged · Carcinoma · Nephrectomy · Thermal ablation · Kidney neoplasms

Abbreviations

ASA	American Society of Anesthesiologists
CA	Cryoablation
CSS	Cancer-specific survival
DFS	Disease-free survival
MW	Microwave
OS	Overall survival
PTA	Percutaneous thermal ablation
RCC	Renal cell cancer
RF	Radiofrequency
RPN	Robot-assisted partial nephrectomy
TTP	Time to progression

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Introduction

Despite the lack of solid evidence, the American and European Urologic Associations recommend percutaneous thermal ablation (PTA) for the treatment of T1 renal cell cancer (RCC) as an option for patients not suitable for surgery [1, 2].

Several comparative studies of matched cohorts have shown differences in overall survival (OS) between patients treated surgically and those treated with PTA [3–6]. However, none of these studies reported a difference in terms of cancer-specific survival (CSS). Furthermore, in the elderly population, studies with matched populations and subgroup analyses [6–9] did not show a difference in terms of OS. This suggests that the difference in OS may result from patients' selection referred to interventional radiology for PTA (older and more frail) rather than from a protective effect of surgery.

Moreover, older patients are a specific population associated with comorbidities and polymedication, which may affect survival benefit in cancer treatment strategy [10, 11]. A thorough risk to benefit ratio must be investigated taking into account their survival benefit but also their quality of life with a faster home recovery. Therefore, minimally invasive options may be of interest.

PTA offers a minimally invasive treatment option with a low rate of morbidity and mortality that can be performed in outpatients under conscious sedation [1, 3, 12, 13]. On the other hand, nephron-sparing surgery has evolved over the last 10 years with the emergence of robot-assisted partial nephrectomy (RPN), which presents better functional results and less postoperative morbidity with similar oncological results than partial nephrectomy (PN) [14, 15].

As so far no guidelines are providing any specific recommendations in patients over 75 years, the objective of this study was to assess and compare the oncological and perioperative outcomes of PTA and RPN in patients older than 75 years.

Materials and methods

Patient selection

All patients were retrospectively included from the French national multicenter prospective database URO-CCR. This project (NCT03293563) was approved by an ethics and research committee and obtained the CNIL authorization number DR-2013-206. The records of all patients older than 75 years at the time of receiving treatment who underwent PTA or RPN for T1 primary renal tumors between January 2010 and January 2021 were retrospectively reviewed. Patients with metastatic disease, suspected of having lymph node metastasis on CT/MRI, less than 75 years of age, insufficient tumor data (histological type or tumor size), multiple tumors on the same kidney, or who underwent concomitant treatment of multiple tumors in the same procedure were excluded. The study flow chart is shown in Fig. 1.

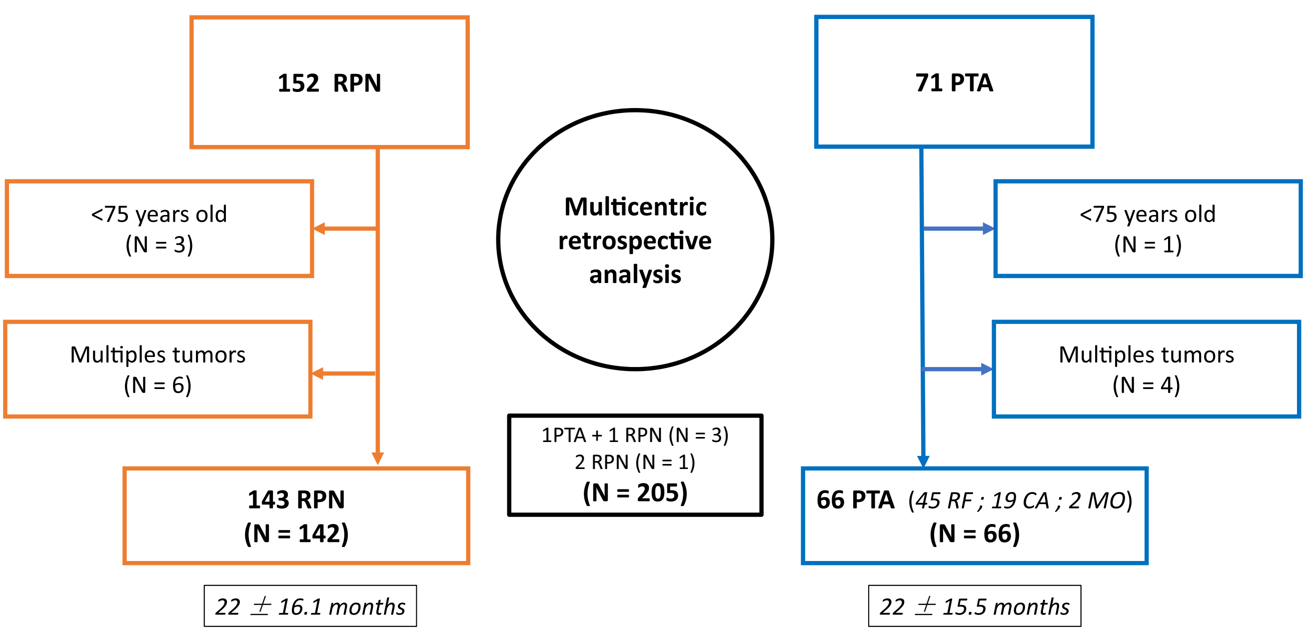


Fig. 1 Study flow chart

Patient characteristics

For all patients, clinical, tumor, and treatment-related characteristics were collected.

Clinical characteristics were gender, age, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and serum creatinine level before and after surgery. Medical history including oncological history, cardiovascular disease, chronic kidney disease, single kidney, and use of anticoagulants or antiplatelet agents was also collected.

Regarding tumor characteristics, preoperative imaging obtained by CT or MRI was used to report tumor size, RENAL score, and laterality. Histologic data were separated into two groups: malignant tumors including clear cell renal cell carcinoma and papillary and chromophobe carcinoma; and benign tumors including angiomyolipoma and oncocytoma.

Operative characteristics were also reported: For each group, total operative time, length of stay, difference in pre- and postoperative serum creatinine level, and use of transfusion during hospital stay were analyzed. Complications were divided into three groups: per-, early-, and late postoperative according to time of onset (perioperative complications were complications that occurred during hospitalization, early postoperative complications were complications that occurred during the first 3 months of follow-up, and late postoperative complications were complications that occurred after).

Nephron-sparing surgery

RPN was performed laparoscopically using Da Vinci generation robots (Intuitive Surgical) as previously described [16]. First, after creating a pneumoperitoneum, the trocars and camera were inserted transperitoneally. After detaching, mobilizing, and displacing the homolateral colon, the renal pedicle was located and then the vessels (vein and then artery) were dissected, isolated, and protected by placement of a Lacs. The dissection of the kidney was limited, in the plane of the simple nephrectomy, respecting the peri-tumoral fat that will be part of the resection specimen.

Percutaneous ablation

All ablations were performed percutaneously under CT, ultrasound, or MRI guidance. Radiofrequency (RF) ablations used multidirectional monopolar electrodes (LeVeen/Boston Scientific; RITA/AngioDynamics) or bipolar systems (Celon/Olympus medical) with or without internal saline cooling system depending on the devices. The number and size of ablation needles were chosen by the operators and ranged from 1 to 3 and from 15 to 50 mm, respectively. The diameter of the needles ranged from 13 to 17 gauges (G). The cryoablations (CA) were performed with the CryoProbe system (Boston Scientific) by applying two freezing (10 to 15 min)-thawing (8 to 10 min) cycles. The type and number of needles were freely chosen by the interventional radiologists according to the location and size of the tumor, ranging from 1 to 5. All devices were 17G in diameter. Microwave (MW) ablations were performed with the Aculis system (AngioDynamics) using a 15-G needle and a generator delivering 60 to 140 W at an operating frequency of 2.45 GHz. The application time was 6 min maximum.

For all ablations, carbo- or hydro-dissection of adjacent organs was performed if necessary. Prior to ablation, a percutaneous renal biopsy for histological analysis was performed prior to the ablation session or just before the procedure the same day.

Follow-up

Local recurrence was defined as the persistence or appearance of enhancement and/or an increase in tumor size. Metastatic disease was defined as progression of extra-renal disease without necessary histological evidence. A new tumor on the contralateral kidney was not considered metastatic progression [17]. Patients whose follow-up was less than 3 months were excluded from the analysis of oncological results. Time to progression (TTP) was defined as the length of time between treatment and local or distant recurrence and disease-free survival (DFS) was defined as the absence of local or distant recurrence and the absence of death.

Statistical analyses

A Shapiro-Wilk test was used to test the distribution of quantitative variables. For the descriptive analysis, the quantitative variables were expressed as mean and standard deviation and the qualitative variables as number and percentage. Quantitative variables were compared with Student's *t*-test and qualitative variables using chi-square or Fisher's test. The duration of follow-up was calculated from the date of treatment until the event or the date of the last follow-up. DFS and overall survival (OS) were analyzed by patient and TTP was analyzed by lesion. Patients who had both PTA and RPN were therefore excluded from the DFS and OS analysis. TTP, DFS, and OS were estimated using the Kaplan-Meier method and group comparison using log-rank or Wilcoxon tests. A Cox proportional hazards regression model was used to measure the association between treatment and oncological outcomes. Considering as acceptable one adjustment factor for 5 events, association between OS and treatment was adjusted for the two most relevant prognostic factors for OS in these patients, namely age and ASA score, and an oncologic factor with tumor size was added for DFS. Likewise, association between TTP and treatment was adjusted for age and history of renal surgery, considering these two factors as the most predictive of recurrence. The corresponding HRs have been calculated and presented with their 95% confidence interval. For all statistical analyses, the level of significance was 0.05.

Results

Population and tumor characteristics

Between January 2010 and January 2021, 205 patients were included for a total of 209 treatments performed: 143 RPN and 66 PTA (RF $n = 45$; CA $n = 19$; MW $n = 2$). One patient had 2 consecutive RPN and 3 patients had both a PTA and a RPN, for a total of 142 different patients in the RPN group and 66 in the PTA group. The mean follow-up was 22 ± 16.1 months [1–68 months] for the RPN group and 22 ± 15.5 months [1–64 months] for the PTA group ($p = 0.98$).

The characteristics of the patients are summarized in Table 1. Patients in the PTA group were older (80.4 ± 3.7 years [75–90 years] vs. 79 ± 3.7 years [75–92 years] for the RPN group, $p < 0.01$). The ASA score was higher in the PTA group (2.43 ± 0.6 [1–4] vs. 2.17 ± 0.6 [1–3] for the RPN group, $p < 0.01$). There was more history of renal surgery in the PTA group (16.7% [11/66] vs. 5.6% [8/142] for the RPN group, $p = 0.02$).

Tumor characteristics are shown in Table 2. Tumors were significantly smaller in the PTA group (2.7 ± 0.7 cm [1.4–4.5 cm] vs. 3.2 ± 0.9 cm [0.9–5.3 cm] for the RPN group, $p < 0.01$). The RENAL score was similar in the two groups (6.1 ± 1.3 [4–10] for the PTA group vs. 6.7 ± 1.8 [4–10] for the RPN group, $p = 0.06$). Most tumors were malignant in both groups: 98% (65/66) in the PTA group and 97% (139/143) in the RPN group. The most common histological type was clear cell carcinoma in both groups with a total of 72% (151/209).

Perioperative and functional results

The perioperative results are shown in Table 3 and Fig. 2. Operative time and length of stay were shorter in the PTA group than in the RPN group, respectively (92.1 ± 42.7 min [27–200 min] vs. 150.7 ± 61.3 min [35–348 min] ($p < 0.01$) and 1.7 ± 1.4 days [1–8 days] vs. 4.2 ± 3.4 days [0–28 days] ($p < 0.01$)). After a mean of respectively 10.8 ± 1 months [13.6–64.7 months] for RPN and 10.6 ± 1 months [14.2–47.6 months] for PTA ($p = 0.93$), the increase in postoperative serum creatinine was higher in the RPN group: 10.1 ± 23.7% [−37 to 81%] vs. 1.9 ± 19.3% [−92 to 59%] in the PTA group (p =0.03). The overall complication rate was similar between groups: 19.6% (13/66) for PTA and 29.4% (42/143) for RPN ($p = 0.1$).

Oncological results

A total of 4 patients (4/66; 6%) in the PTA group and 18 patients (18/142; 12.7%) in the RPN group had less than 3 months follow-up and were therefore excluded. Three patients (3/183; 1.6%) underwent both RPN and PTA and were excluded from the DFS and OS analyses. The number of

Table 1 Characteristics of > 75-year-old patients with renal tumor scheduled for treatment

Patients' characteristic	Thermoablation ($n = 66$)	Robotic partial nephrectomy ($n = 142$)	p
Age (years)	80.4 ± 3.7 [75–90]	79 ± 3.7 [75–92]	0.01*
Male	69.6% (46/66)	67.1% (96/142)	0.7
Body mass index (kg.m^2)	27.1 ± 4.5 [15.1–38.5]	26.8 ± 4.8 [14.2–45.4]	0.2
ASA score	2.43 ± 0.6 [1–4]	2.17 ± 0.6 [1–3]	< 0.01*
Single kidney	12% (8/66)	6.3% (9/142)	0.15
Renal function impairment	12.1% (8/66)	5.6% (8/142)	0.1
Cardiovascular disease	77.3% (51/66)	80.1% (115/142)	0.5
Anticoagulation or antiplatelet therapy	24% (16/66)	23.7% (34/142)	0.9
Other cancer	37.9% (25/66)	35.2% (50/142)	0.9
History of kidney surgery	16.7% (11/66)	5.6% (8/142)	0.02*
Preoperative creatinine serum level	94.2 ± 35.5 [47.8–268]	88.9 ± 25 [46–193]	0.3

ASA, American Society of Anesthesiologists

Quantitative variables are expressed as means ± standard deviations; numbers in brackets are ranges. Qualitative variables are expressed as proportions; numbers in parentheses are percentages. *Student's *t*-test for quantitative variables and chi-square for qualitative variables; significant p value < 0.05

Table 2 Characteristics of the tumors of > 75-year-old patients scheduled for treatment

Tumor's characteristic	Thermoablation (n = 66)	Robotic partial nephrectomy (n = 143)	p
Size (in cm)	2.7 ± 0.7 [1.4–4.5]	3.2 ± 0.9 [0.9–5.3]	< 0.01*
RENAL score	6.1 ± 1.3 [4–10]	6.7 ± 1.8 [4–10]	< 0.05
Malignant	98.5% (65/66)	97.2% (139/143)	0.8
Clear cell renal cell carcinoma	78.8% (52/66)	69.2% (99/143)	0.4
Papillary carcinoma	7.6% (5/66)	15.4% (22/143)	0.1
Chromophobe renal carcinoma	1.12% (8/66)	12.6% (18/143)	0.9
Oncocytoma	1.5% (1/66)	2.8% (4/143)	0.6

Quantitative variables are expressed as means ± standard deviations; numbers in brackets are ranges. Qualitative variables are expressed as proportions; numbers in parentheses are percentages. *Student's t-test for quantitative variables and chi-square for qualitative variables; significant p value < 0.05

local recurrences was higher in the PTA group although not significant (12.9% (7/62) vs. 4.8% (6/125) in the RPN group, $p = 0.13$), and the number of distant recurrences was similar, respectively (6.5% (4/62) in the PTA group vs. 6.4% (8/125) in the RPN group, $p = 1$). TTP was similar between groups: 57.3 months for patients in the RPN group and 45 months for those in the PTA group ($p = 0.11$; Fig. 3), even after adjusting for tumor size and a history of renal surgery (HR 2.1; 95% CI [0.86–5.2]; $p = 0.1$). A total of 15 patients died: 9 in the PTA group (9/59; 15.2%) and 5 in the RPN group (5/121; 4.1%) ($p = 0.02$). In terms of OS, there was a difference in univariate analysis in favor of RPN (56.9 vs. 46.9 months, $p = 0.03$; Fig. 4). After adjusting for age and ASA score, this difference was not found (HR 3.3; 95% CI [0.87–12.72]; $p = 0.08$). DFS was not significantly different between the groups, respectively (53 months for RPN and 41 months for PTA ($p = 0.05$; Fig. 5)) even after adjusting for age, ASA score, and height of the tumor (HR 2.2; 95% CI [0.88–5.5]; $p = 0.09$).

Discussion

After adjustment for age, ASA score, tumor size, and history of renal surgery, oncological results between RPN and PTA were similar in this cohort of patients aged over 75 years. The length of hospital stay and the loss of renal function were significantly inferior in the PTA group, with similar postoperative complications rates.

In terms of outcomes, DFS and TTP were higher in the RPN group compared to the PTA group with no significant difference (respectively 53 vs. 41 months, $p = 0.05$; 57.3 vs. 45 months, $p = 0.11$). Similar oncological results in elderly patients have already been reported in the literature [9]. Cholley et al reported in the same population a TTP of 30 months in the PN group vs. 26 months in the PTA group (log-rank $p = 0.52$) and an OS of 42 months in the PN group vs. 30 months in the PTA group, with no significant difference after model adjustment (HR 2.37, $p = 0.19$). Studies

Table 3 Characteristics of intervention

Interventions' characteristic	Thermoablation (n = 66)	Robotic partial nephrectomy (n = 143)	p
Total operation time (min)	92.1 ± 42.7 [27–200]	150.7 ± 61.3 [35–348]	< 0.01*
Length of hospital stay (days)	1.7 ± 1.4 [1–8]	4.2 ± 3.4 [0–28]	< 0.01*
Postoperative increase in serum creatinine level (in %)	1.9 ± 19.3 [−92 to 59]	10.1 ± 23.7 [−37 to 81]	0.03*
Postoperative transfusion	2% (1/66)	3% (4/143)	0.6
Complications	6% (4/66)	13.3% (19/143)	0.1
•Perioperative	6% (4/66)	2.8% (4/143)	0.2
•Postoperative	7.6% (5/66)	13.3% (19/143)	0.2
•Late	**19.6% (13/66)**	**29.4% (42/143)**	0.15
•Total			

Quantitative variables are expressed as means ± standard deviations; numbers in brackets are ranges. Qualitative variables are expressed as proportions; numbers in parentheses are percentages. *Student's t-test for quantitative variables and chi-square for qualitative variables; significant p value < 0.05

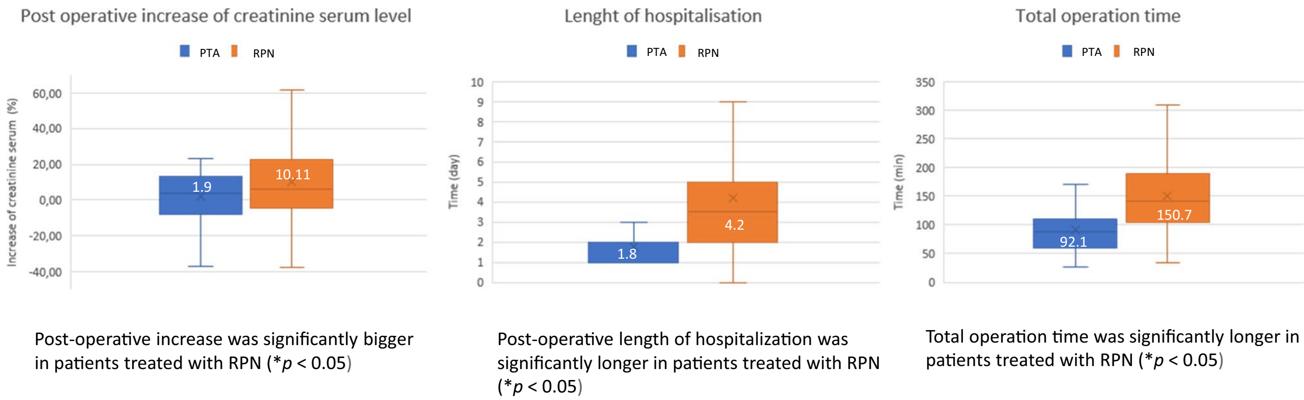
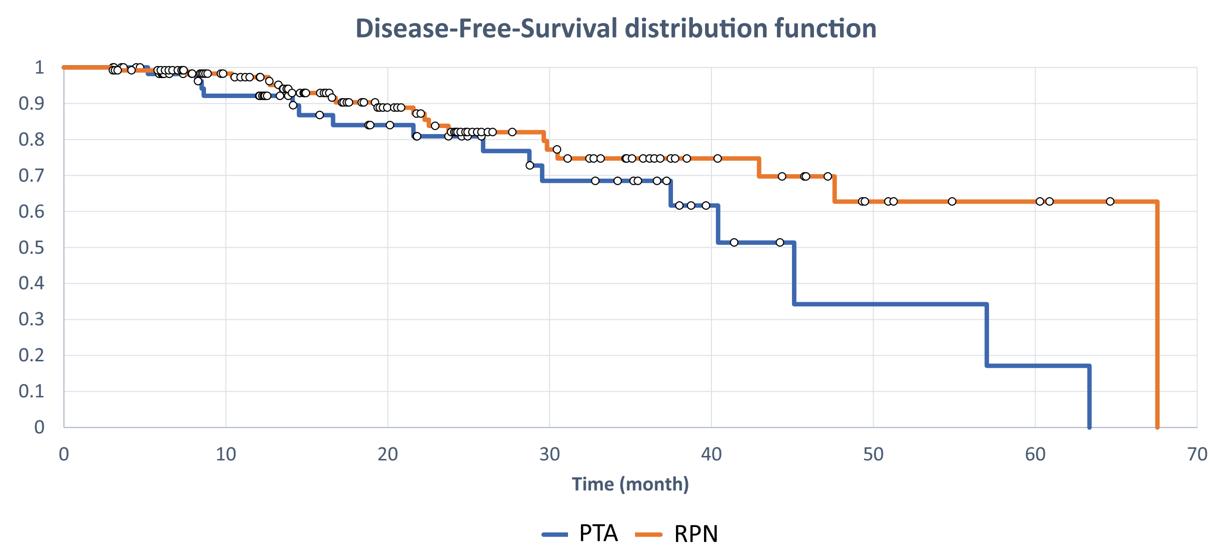


Fig. 2 Boxplots of perioperative outcomes for each group. RPN, robotic partial nephrectomy; PTA, percutaneous ablation

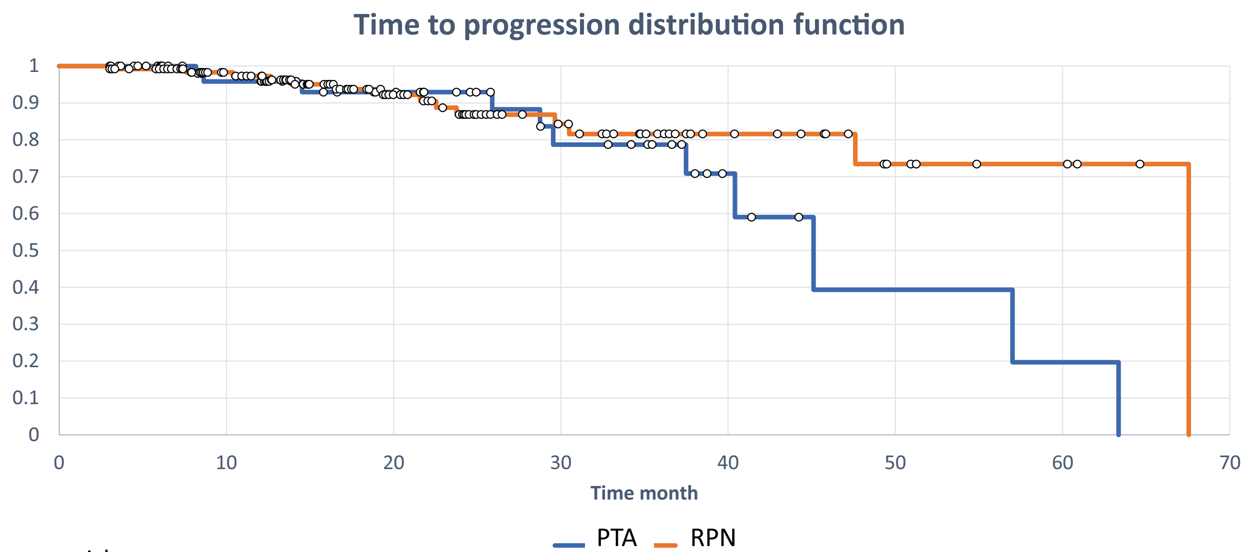
comparing the two techniques in the general population are more heterogeneous. Indeed, the study by Pantelidou et al found a 5-year PFS with similar results (HR = 0.84, 95% Cl 0.19–3.4; $p = 0.80$), whereas other studies, notably Park et al [18] and Tanagho et al [19] report better results for surgery with a 2-year RFS of 95.2% vs. 100% ($p = 0.03$) and a DFS at 5 years of 83.1% vs. 100% ($p < 0.05$). However, as shown by Kutikov et al [10], the impact on OS of a recurrence in elderly patients seems less significant than in the general population. Furthermore, since PTA is easily repeatable, those patients may benefit from a retreatment with similar morbi-mortality than the first treatment [18]. In univariate analysis, a better OS was found in the RPN group (56.9 vs. 46.9 months, $p = 0.03$). However, after adjusting for age and ASA score, this difference was not found (HR 3.32; 95% CI [0.87–12.72]; $p = 0.09$). Although several comparative studies of matched cohorts have also shown differences in OS between patients treated surgically and those treated with PTA [3–5], with HRs ranging from HR = 1.44, $p = 0.0457$ to HR = 2.33, $p < 0.001$. However, none of these studies



Patients at risk

Time *(months)*	10	20	30	45	60
PTA	49	28	17	3	1
RPN	98	58	34	13	4

Fig. 3 Disease-free survival after robot-assisted partial nephrectomy (RPN) and percutaneous thermoablation (PTA). Mean survival time was 53 months for PN patients and 41 months for PTA patients (log-rank test $p = 0.053$). Dots indicate censored patients



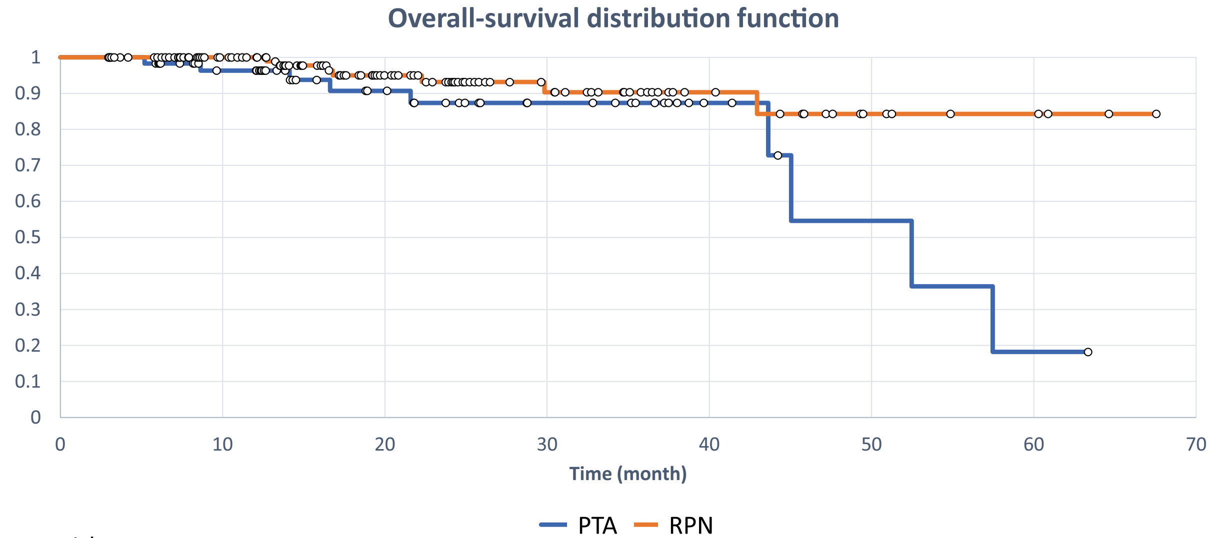
Patients at risk

Time *(months)*	10	20	30	45	60
PTA	45	28	17	3	1
RPN	98	58	34	13	4

Fig. 4 Time to progression after robot-assisted partial nephrectomy (RPN) and percutaneous thermoablation (PTA). Mean survival time was 57.28 months for PN patients and 45 months for PTA patients (log-rank test $p = 0.11$). Dots indicate censored patients

reported a difference in terms of cancer-specific survival. In addition, studies with matched populations and subgroup analyses in elderly patients [6–8, 20] did not show a difference in terms of OS. This suggests that the difference in OS results from patients' selection referred to interventional radiology (older and more frail) rather than from a protective effect of surgery. These results are consistent with those of Kutikov et al [11] and Lane et al [21] who demonstrated that age and comorbidities increased the risk of death from other causes in patients with small kidney cancers. Conversely, Morkos et al [12] reported after matching and multivariate analysis a better OS after PTA using CA suggesting a better outcome for patients treated with CA. However, no study demonstrated a superiority in terms of oncologic outcome favoring an ablative technique for T1a RCC [22]. In the present study, patients in the PTA group were older, had more comorbidities, were treated for smaller tumors, and had more often a history of previous renal surgery. These results are also found in the most recent cohort studies on the same study population [4, 8, 12, 23].

Regarding renal function, a significantly better preservation was observed in the PTA group than in the RPN group with 10% increase in the RPN group vs. only 1.9% in the PTA group. However, both techniques offered good results on postoperative creatinemia. These results had already been presented in the general population [19, 24], notably in a meta-analysis [25] with a weighted mean difference of −8.06 mL/min/1.73 m between groups ($p = .04$), but never in this subpopulation of elderly patients. Since we know the potential cardiovascular impact and risks of drug toxicity related to a decrease in renal function in these patients, the use of both techniques should be recommended to improve patients' outcome, favoring PTA in case of severe renal failure [26]. The overall complication rate was higher in this study population than in other studies comparing these two approaches (29.4% for RPN and 19.6% for PTA vs. 17% and 8% in the study of Pantelidou et al [24] and 10.1% and 14.8% in the meta-analysis of Yoon et al [25]). This can be explained by patients' frailty in this study on older patients compared to the general population. In this study, the perioperative results were better for PTA in terms of length of hospital stay and operative time, consistently with previous studies [25, 27]. These results suggest that PTA permits a substantial reduction in the occupancy time of the operating rooms, and consequently a potential reduction in the costs of patient care [27, 28]. On the other hand, the length of hospital stay reduction is important in these elderly patients who can decompensate another pathology during their hospital stay, which could trigger lethal worsening of their condition. Consequently, in frail older patients, PTA offers an advantage over RPN with



Patients at risk

Time *(months)*	10	20	30	45	60
PTA	49	28	18	5	1
RPN	99	58	32	12	4

Fig. 5 Overall survival after robot-assisted partial nephrectomy (RPN) and percutaneous thermoablation (PTA). Mean survival time was 46.9 months for PTA vs. 56.9 months in the PN group (log-rank test $p = 0.031$). Dots indicate censored patients

a faster home recovery that may result in a survival benefit but also in an improvement of life's quality.

This study has several limitations. First, this is a retrospective analysis of a prospective cohort with a limited number of patients, especially for PTA. The diagnosis of oncocytoma treated with PTA relying on a core biopsy is limited. However, only one patient had oncocytoma in the PTA group and no recurrence was observed. CSS was not studied in this cohort due to the lack of events and data on the causes of death. Although the populations were significantly different with notably younger and healthier patients in the RPN group, a population matching could not be performed due to the relatively small number of patients. We also did not perform a subgroup analysis, particularly of the different ablation techniques, given the small sample and the low number of events. We therefore considered that all the techniques were equivalent in terms of efficacy for small renal masses. Finally, the number of patients lost to follow-up was relatively high, particularly in the RPN group.

In conclusion, this study compared the robot-assisted NSS and the PTA approach specifically on this elderly population over 75 years. The results show that PTA and RPN are safe and effective treatments for T1 kidney cancer in elderly patients, with similar oncological outcomes. The operative time, the decrease in renal function, and the length of hospital stay were lower with PTA. The choice of treatment strategy in a curative intent should then rely on patients' comorbidity, age, and progression-risk and incorporate in future guidelines.

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Declarations

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Informed consent Written informed consent was waived by the institutional review board.

Ethical approval All patients were retrospectively included from the French national multicenter prospective database URO-CCR. This project (NCT03293563) was approved by an ethics and research committee and obtained the CNIL authorization number DR-2013-206.

Study subjects or cohorts overlap None.

Methodology
- Retrospective
- Observational
- Multicenter study

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