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**Perioperative outcomes following robot-assisted partial nephrectomy in elderly patients**

**Running title: Robot-assisted partial nephrectomy in elderly patients.**

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**Abstract**

**Objective:** To compare perioperative outcomes following robot-assisted partial nephrectomy (RAPN) in patients with age ≥70 years to age < 70 years.

**Methods:** Using Vattikuti Collective quality initiative (VCQI) database for RAPN we compared perioperative outcomes following RAPN between the two age groups. Primary outcome of the study was to compare trifecta outcomes between the two groups. Propensity matching using nearest neighbourhood method was performed with trifecta as primary outcome for sex, body mass index (BMI), solitary kidney, tumor size and Renal nephrometery score (RNS).

**Results:** Group A (age ≥ 70 years) included 461 patients whereas group B included 1932 patients. Before matching the two groups were statistically different for RNS and solitary kidney rates. After propensity matching, the two groups were comparable for baselines characteristics such as BMI, tumor size, clinical symptoms, tumor side, face of tumor, solitary kidney and tumor complexity. Among the perioperative outcome parameters there was no difference between two groups for operative time, blood loss, intraoperative transfusion, intraoperative complications, need for radical nephrectomy, positive margins and trifecta rates. Warm ischemia time was significantly longer in the younger age group (18.1 mins vs. 16.3 mins, p=0.003). Perioperative complications were significantly higher in the older age group (11.8% vs. 7.7%, p=0.041). However, there was no difference between the two groups for major complications.

**Conclusion:** RAPN in well-selected elderly patients is associated with comparable trifecta outcomes with acceptable perioperative morbidity.

**Keywords:** robotic; partial nephrectomy; elderly; propensity-matching.

## Introduction

Partial nephrectomy (PN) as a treatment option for small localized renal masses has become the standard of care[1]. Utilization rates of partial nephrectomy for renal masses have increased across all age groups[2, 3]. Superior functional and comparable oncological outcomes for PN compared to radical nephrectomy (RN) have translated into increased adoption of PN[4, 5]. In recent years, there has been a trend toward increased utilization of partial nephrectomy as a treatment option for managing localized small renal masses[6, 7]. However, its utilization in the elderly population remains poor[2, 3]. Reasons for this underutilization could be manifold. There is little doubt about the efficacy of partial nephrectomy in renal function preservation compared to RN[8-10]. However, elderly patients are at a significantly higher risk of death due to competing causes of mortality. Therefore, they may not extract long-term cardiovascular benefits from renal function

preservation. Thus, the lack of proven benefits in terms of overall and cancer-specific survival may be one of the deterrents for undergoing PN in the elderly population[9-12].

Some studies have even reported superior overall survival due to a decrease in other causes of mortality such as cardiovascular events due to better renal function preservation with PN[13, 14]. However, this comes at the expense of increased perioperative complications associated with PN[15-17]. The apprehension of increased complications without any proven oncological benefit has led to a lower acceptance of PN for the elderly patient population. Population-based studies have shown lower rates of increased adoption of PN for elderly patients compared to their younger counterparts[2, 3]. Literature on perioperative outcomes following PN for the elderly population is limited. Furthermore, non-invasive treatment options as focal therapy has provided an alternative to PN in frail elderly patients with comorbidities[1].

Few studies have reported outcomes following robot-assisted partial nephrectomy (RAPN) in the elderly population[18-20]. These studies have reported acceptable outcomes following RAPN in well-selected elderly patients. However, none of these studies have compared results with younger patients. Hence, with this Vattikuti collective quality initiative (VCQI) database study, we aimed to compare perioperative outcomes between patients aged ≥70 years and < 70 years following RAPN.

## Materials and Methods

### Vattikuti Collective Quality Initiative (VCQI) database

VCQI is a prospective web-based multi-institutional collaborative database for various robotic surgical procedures[21-24]. Details of centers contributing to the database is provided in the supplementary file. Ethics clearance was obtained from each participating institution prior to data sharing. Due to the multi-institutional nature of the database, patients without adequate data had to be excluded from the study. For every patient, demographic, perioperative and postoperative data were collected as detailed in Table 1. Perioperative complications were graded as per Clavien-Dindo classification[25]. The primary objective of this study was the comparison of trifecta outcomes

between patients over the age of 70 years and those aged less than 70 years. Subgroup analysis of patients over the age of 80 years and those aged less than 80 years was also performed. Trifecta outcome was achieved without any complications, negative surgical margins, and warm ischemia time ≤ 25 minutes or zero ischemia[24, 26].

**Statistical analysis**

We checked the normality of continuous data using Kolmogorov-Smirnov and Shapiro tests of normality. An independent sample Student's t-test was used if data were normally distributed. Kruskal-Wallis test was used for non-normally distributed variables. For categorical variables, chi-square tests or Fisher's exact tests were used. Propensity matching using the nearest neighborhood method was performed with trifecta as the primary outcome for sex, BMI, solitary kidney, tumor size and RNS. All the statistical tests were two-sided and performed with a significance level of $p < 0.05$. The statistical tests were double-sided and conducted using SPSS version 23 (IBM corporation, New York, USA) and Stata (version 16; StataCorp, College Station, TX, USA). A p-value performed $< 0.05$ was used to define significance.

**Results**

From October 2014 to 2020, the participating centers contributed data of 3,801 patients who underwent RAPN. Of the 3,801 patients, 2,393 patients with complete data were included for the final analysis.

**Prematching**

Group A (age ≥ 70 years) included 461 patients, whereas group B included 1932 patients. A comparison of two groups for baseline factors revealed that the two groups were comparable for sex, BMI and clinical tumor size. Mean age in A group was 75.1 years and 52.8 years (p=0.000) in group B. There was no significant difference between the two groups for clinical symptoms, side of tumor, face of tumor, polar location of tumor and number of lesions operated. However, group A included a significantly higher number of patients with solitary kidneys (4.7% vs. 1.96%, p=0.000). The mean RNS score was higher in group B patients (7.07 vs 6.88, p=0.03). Group B

also had a significantly higher number of patients in the 'high complexity' stratification of RNS (10.4% vs. 6.3%). Preoperative hemoglobin (12.98 vs. 13.4, p=0.000), and eGFR (68.4 vs. 83.5, p=0.000) were significantly lower in group A, whereas creatinine was significantly higher in group A (1.08 vs. 0.94, p=0.000) (Table 1).

In comparison of operative variables, two groups were comparable for surgical access (transperitoneal or retroperitoneal), duration of surgery, blood loss, positive margin intraoperative transfusion and intraoperative complications. Conversion to radical was significantly higher in the older age group (2.4% vs. 0.9%, p=0.010) (Table 1). The postoperative complication rate was significantly higher in group older age group (12.5% vs. 7.8%, p=0.001). However, the rate of major (grade III/IV) complications was similar in the two groups (2.6% vs. 2%, p=0.841). Overall, major complications were noted in 52 of the patients. Among the patients with major complications, organ failure/ need for intensive care was required in 11 patients. Angioembolization was needed in 21 patients, 11 patients required Double J stenting for urine leak and rexploration was needed in 9 patients.The two groups showed no statistically significant difference for trifecta (71.5% vs. 71.1%, p=0.860).

**Postmatching**

Propensity matching was possible for 440 patients in either group. After propensity matching, the two groups were comparable for baseline characteristics such as BMI, tumor size, clinical symptoms, tumor side, face of tumor, solitary kidney and tumor complexity (Table 2). Among the perioperative outcome parameters there was no difference between the two groups for operative time, blood loss, intraoperative transfusion, intraoperative complications, need for radical nephrectomy, positive margins and trifecta rates. Warm ischemia time was significantly longer in the younger age group (18.1 mins vs. 16.3 mins, p=0.003). Perioperative complications were significantly higher in the older age group (11.8% vs. 7.7%, p=0.041). However, there was no difference between the two groups for major complications. On multivariate analysis, gender, tumor size and renal nephrometery score were identified as independent predictors of trifecta (Table 3).Standardized mean differenced and variance ratios for the continuous covariates postmatching have been provided in the supplementary table.

**Subgroup analysis**

Comparison of patients aged more than 80 years (n = 69) and less than 80 years (n= 2,324) showed that the two groups were comparable for certain baseline characteristics such as tumor size, sex, clinical symptoms, tumor side, face of tumor, tumor location, solitary kidney and tumor complexity (Table 4). There was no difference between the two groups for operative time, blood loss, intraoperative transfusion, intraoperative complications, need for radical nephrectomy, positive margins and trifecta rates. Warm ischemia time was significantly longer in the younger age group (18 mins vs. 14.2 mins, p=0.001). Perioperative complications were significantly higher in the older age group (16% vs. 8.5%, p=0.031). However, there was no difference between the two groups for major complications (2.9% vs. 2.1%, p=0.675).

## Discussion

In the present study, before matching the two age groups were comparable in sex, BMI and clinical tumor size. However, the two groups differed significantly for Charlson comorbidity index, solitary kidney rates and renal nephrometery scores. There was no difference in the two groups for operative time, intraoperative complications, need for blood transfusion and blood loss. Mean WIT was significantly longer in the younger age group (18.3± 9.26 vs. 16.2± 8.7, p=0.000). Mean WIT remained longer in the younger age group even after matching. Furthermore, the conversion to radical nephrectomy was significantly higher in the elderly age group. However, there was no difference between the two groups for conversion to radical nephrectomy after matching (2% vs. 1.1%, p=0.281). We noted significantly higher complications in group A (age ≥70 years) in the present study (before and after matching). However, this increased predilection was limited to the minor complications (grade 1 and 2), with rates of major complications being the same between the two groups. Similar results were noted when we compared for subgroup analysis for patients with age greater and lesser than 80 years. Literature is divided on the complication rates following PN compared to RN. Some studies have reported similar[27-29] and others have reported increased[15,17] complications in patients undergoing PN compared to RN irrespective of the age group. A similar predicament related to complication rates for PN compared to RN is noted in studies reporting outcomes specifically in the elderly population. Two studies have reported (Lowrance et al[30] and Veccia et al[12]) significantly higher complication rates for elderly patients who underwent

PN compared to RN. However, An et al[10] and Antonelli et al[8] reported similar complications between RN and PN in their patient cohort.

Only a handful of studies have previously reported outcomes of PN in the elderly patient population[12, 18-20]. In their cohort of patients with a median age of 78 years, Ingels et al reported rates of blood transfusion, trifecta, intraoperative complications and major complications of 14.7%, 45%, 9% and 6.2%, respectively[18]. In contrast, patients above ≥ 70 years in the present study had much higher trifecta rates (71.5%) with lower perioperative morbidity. However, it is to be pointed out that in the study by Ingels et al different surgical modalities (open, laparoscopic and robotic) were employed and a robotic approach was predictive of lower complication rates[18]. In their cohort of elderly patients who underwent RAPN, Vartolomei et al reported perioperative outcomes similar to the present study[20]. Authors reported median operative time, blood loss, warm ischemia time and length of stay of 180 minutes, 100 ml, 14.5 minutes, and 5 days respectively. Positive surgical margins, overall complications and trifecta outcomes were reported in 1.9%, 15.4% and 71.2% respectively[20]. Similar results were reported by Bindayi et al. in their study for PN in their cohort of elderly patients[19]. Veccia et al compared RAPN to robotic RN in patients older than 65 years of age[12]. Authors reported positive surgical margin, overall complications, major complications and blood transfusion rates as 6%, 24%, 19% and 6%, respectively, in the RAPN group[12]. Superior rates of these perioperative outcomes were noted in the present study. Results of RAPN stated in the present study for the elderly group compare well for perioperative outcomes of the contemporary RAPN series[31-34].

Our study is not without limitations. Firstly, due to the study's retrospective nature, the probability of a selection bias in patient inclusion is high. This is highlighted by the fact that elderly patients had lower complexity tumors in general, as compared to the matched cohort of younger patients. Propensity-matching between the two groups was performed to make two groups comparable for baseline factors. Furthermore, of the 3,801 patients, we included only 2,393 patients with complete data in this study. This could be one of the major limitations of this study. Secondly, the VCQI database also lacks surgeon experience or center caseload data. Lastly, Thirdly, there is heterogeneity in surgical techniques, learning curves, and perioperative management of patients due to the broader reach of the VCQI database However, for precisely the same reasons, we believe

that our study is closer to the ‘real world scenario’ of the outcomes of RAPN in elderly patients and may provide unique insights regarding the same.

## Conclusion

Robot-assisted partial nephrectomy in well-selected elderly patients may be associated with comparable trifecta outcomes. However, the rates of overall perioperative complications were significantly higher in the elderly patient population.

## DECLARATIONS

### Statements and Declarations

### Authors contribution

All the authors were involved in data acquisition and manuscript editing. G.S, M.S, P.A & G.G were involved in conception, design, analysis, manuscript writing and editing. G.G was involved in supervision of the project.

### Compliance with Ethical Standards

Conflict of interests: Ronney Abaza is a speaker for Intuitive surgical, Conmed Inc and VTI. Benjamin J Challacombe, Kris K Maes, Rajesh Ahlawat and Gagan Gautam are proctors for Intuitive surgical. Other authors report no conflict of interests.

**Research involving Human Participants and/or Animals:** This study is retrospective analysis of VCQI database and ethics approval was obtained from all the participating centers prior to data collection.

**Informed consent:** Need for consent waived off by ethics committee.

**Data availaibility statement:** Corresponding author had full access to data and same can be provided on request to genuinine authors.

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**Table legends**

**Table 1:** Comparison of baseline characteristics between the two age groups (Age ≥70 years and <70 years)

**Table 2:** Comparison of perioperative outcomes between the two age groups post matching (Age ≥70 years and <70 years).

**Table 3:** Multivariate analysis for the predictors of the trifecta outcomes.