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Is Robot-assisted Surgery Contraindicated in the Case of Partial Nephrectomy for Complex Tumours or Relevant Comorbidities? A Comparative Analysis of Morbidity, Renal Function, and Oncologic Outcomes

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Abstract

Background: Available comparisons between open partial nephrectomy (OPN) and robot-assisted partial nephrectomy (RAPN) are scarce, incomplete, and affected by non-negligible risk of bias.

Objective: To compare RAPN and OPN.

Design, setting, and participants: This was an observational study of 472 patients diagnosed with a cT1–2cN0cM0 renal mass and treated with RAPN or OPN assessed in two prospective institutional databases.

Outcome measurements and statistical analysis: The study outcomes were morbidity, complications, warm ischaemia time, renal function, positive surgical margins, and oncologic outcomes. Propensity score matching for age at diagnosis, gender, Charlson comorbidity index, preoperative estimated glomerular filtration rate (eGFR), single kidney status, tumour size and side, total PADUA score, any individual PADUA score item, and year of surgery was used to account for baseline confounders. The effect of surgical approach was estimated using linear and logistic regressions for continuous and categorical outcomes. An interaction test was used for subgroup analyses.

Results and limitations: Relative to OPN, RAPN was associated with lower rates for overall (21% vs 36%; $p < 0.0001$) and major (3% vs 9%; $p = 0.03$) complications. This benefit was consistent in patients with high PADUA scores, high CCI, large tumours, and low preoperative eGFR (all $p > 0.05$, interaction test). No difference between the groups was observed for warm ischaemia time, postoperative and 1-yr eGFR, and positive surgical margins (all $p > 0.05$). After median follow-up of 41 mo, there was no difference between the groups for the 5-yr rates of local recurrence-free, systemic progression-free, and disease-free survival (all $p > 0.05$).

Conclusions: RAPN is associated with overall better perioperative morbidity and lower rates of complications, regardless of characteristics such as tumour complexity and patient comorbidity status. Functional and oncologic outcomes are equal after RARP and OPN.

Patient summary: Robot-assisted partial nephrectomy is associated with a better morbidity profile than open partial nephrectomy (OPN) and provides the same cancer control and renal function preservation observed after OPN.

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1. Introduction

Nephron-sparing surgery represents the standard of care for active treatment of patients diagnosed with a cT1 renal mass [1–3]. Since its first description [4], the adoption of robot-assisted partial nephrectomy (RAPN) has gained remarkable momentum, with a 45% relative annual increase from 2008 to 2010 in the USA [5].

To date, comparisons between open partial nephrectomy (OPN) and RAPN are scarce, affected by a non-negligible risk of bias owing to a lack of detailed information about tumour anatomic complexity and incomplete data for postoperative renal function and oncologic outcomes assessment. Therefore, evidence generating definitive recommendations regarding the surgical approach for PN is not available [6,7] and current guidelines do not favour a specific surgical approach in the decision between OPN and RAPN.

For this reason, the current study relied on two prospectively collected institutional databases to perform a comprehensive comparison of perioperative morbidity, renal function, and oncologic outcomes following RAPN or OPN after the most precise adjustment for patient and tumour preoperative characteristics. We hypothesised that RAPN is associated with lower perioperative morbidity and similar functional and oncologic outcomes relative to OPN.

2. Patients and methods

2.1. Study population

Clinical data were prospectively collected for 472 patients diagnosed with a cT1–2 cN0 cM0 renal mass at computed tomography or magnetic resonance imaging and treated at IRCCS Ospedale San Raffaele (170 OPN, 84 RAPN) and Onze Lieve Vrouw Ziekenhuis (218 RAPN) from 2005 to 2016 by surgeons with extensive PN experience. The approach was selected according to the surgeon's choice. To precisely measure tumour anatomic complexity using an established classification system [8], cases with multiple tumours were excluded. Non-naïve patients with a previous history of kidney cancer were also excluded. For the same reason, cases without availability of preoperative imaging were also excluded.

2.2. Outcomes

The study outcomes were as follows:

1. Morbidity and complications: overall and grade-specific complications according to the Clavien-Dindo (CD) classification [9].
2. Functional outcomes: warm ischaemia time, postoperative estimated glomerular filtration rate (eGFR) defined according to the Chronic Kidney Disease Epidemiology Collaboration equation for patients aged <70 yr and the Berlin Initiative Study formula for patients aged ≥ 70 yr [10] and measured at the last determination before discharge and 1 yr after surgery.
3. Pathologic and oncologic outcomes: positive surgical margins, local recurrence-free survival (RFS; defined as evidence of disease in the resection bed), systemic progression-free survival (PFS; defined as evidence of disease elsewhere than the treated kidney), and disease-free survival (DFS; defined as combination of RFS and systemic PFS.

2.3. Covariates

Covariates consisted of age at diagnosis, gender (male vs female), Charlson comorbidity index (CCI) [11], preoperative eGFR, single kidney status, clinical tumour size (defined as the greatest tumour diameter in millimetres at preoperative imaging), clinical tumour stage (cT1a vs cT1b vs cT2 defined according to the American Joint Committee on Cancer manual [12]), tumour side (left vs right), and year of surgery. Tumour complexity was determined by the urologist and was defined using total PADUA score [8] and any individual PADUA score item, namely longitudinal location, rim location, renal sinus involvement, relationship with urinary collecting system, and exophytic rate. Cases treated after 2009 were assessed before surgery and prospectively collected; cases treated earlier were retrospectively evaluated.

2.4. Statistical analyses

Statistical analyses and reporting and interpretation of the results were conducted according to established guidelines [13] and consisted of four steps. First, the median and interquartile range and the frequency and proportion were reported for continuous and categorical variables, respectively. Mann-Whitney and χ^2 tests were used to compare the statistical significance of differences in the distribution of continuous and categorical variables, respectively, between the OPN and RAPN groups.

Second, to account for any potential baseline differences between OPN and RAPN patients, adjustment was performed using 1:1 nearest-neighbour propensity score matching [14]. Propensity scores were computed using a logistic regression model with the odds of receiving OPN as the dependent variable and age at diagnosis, gender, CCI, preoperative eGFR, single kidney status, clinical tumour size, tumour side, total PADUA score, any individual PADUA score item, and year of surgery as the independent variables.

Third, after estimation of covariates balanced between the matched groups [15], the effect of surgical approach (RAPN vs OPN) on study outcomes was estimated using linear and logistic regression for continuous and categorical outcome variables, respectively.

Fourth, the hypothesis that the effect of surgical approach on complications differed by selected subgroups, namely cases with high PADUA score, high CCI, large tumours, and low preoperative eGFR, was tested using an interaction term between treatment type (RAPN vs OPN) and PADUA score, CCI, clinical tumour size, and preoperative eGFR on an individual basis. Regression-derived coefficients were used to estimate the overall complication risk following RAPN or OPN. A locally weighted scatter plot smoothing method [16] was used to graphically explore the risk of overall complications according to PADUA score, CCI, clinical tumour size, and preoperative eGFR.

All statistical tests were performed using the RStudio graphical interface v.0.98 for R software environment v.3.0.2 [17] with the following libraries, packages and scripts: *Hmisc*, *plyr*, *stats*, *MatchIt*, *rms*, and *graphics*. All tests were two-sided with the significance level set at $p < 0.05$.

3. Results

3.1. Patient characteristics

Overall, 472 patients were included in the study (Table 1). In the cohort before propensity score matching, patients treated with RAPN were diagnosed with a smaller tumour (3.5 vs 3 cm; $p = 0.01$) relative to patients treated with OPN. In the cohort after propensity score matching, there was no difference between the RAPN and OPN groups with respect to all the covariates evaluated (all $p > 0.05$).

3.2. Morbidity and complications

In the cohort after propensity score matching (Table 2), relative to the OPN group, patients treated with RAPN had a lower risk of overall complications (21% vs 36%; odds ratio