R-LESS Partial Nephrectomy Trifecta Outcome Is Inferior to Multiport Robotic Partial Nephrectomy: Comparative Analysis

Christos Komninos\textsuperscript{a,b}, Tae Young Shin\textsuperscript{c}, Patrick Tuliao\textsuperscript{a}, Young Eun Yoon\textsuperscript{a}, Kyo Chul Koo\textsuperscript{a}, Chien-Hsiang Chang\textsuperscript{a}, Sang Woon Kim\textsuperscript{a}, Ji Yong Ha\textsuperscript{a}, Woong Kyu Han\textsuperscript{a}, Koon Ho Rha\textsuperscript{a,*}

\textsuperscript{a}Department of Urology and Urological Science Institute, Yonsei University College of Medicine, Seoul, South Korea; \textsuperscript{b}Department of Urology, General Hospital of Nikaia ’St. Panteleimon’, Athens, Greece; \textsuperscript{c}Department of Urology, Chuncheon Sacred Hospital, Hallym Medical College, Chuncheon, South Korea

Abstract

\textbf{Background:} Trifecta achievement in partial nephrectomy (PN) is defined as the combination of warm ischemia time ≤20 min, negative surgical margins, and no surgical complications.

\textbf{Objective:} To compare trifecta achievement between robotic, laparoendoscopic, single-site (R-LESS) PN and multiport robotic PN (RPN).

\textbf{Design, setting, and participants:} Data from 167 patients who underwent RPN from 2006 to 2012 were retrospectively analyzed.

\textbf{Outcome measurements and statistical analysis:} Primary outcome measurement was trifecta achievement; secondary outcome was the perioperative and postoperative comparison between groups. The measurements were estimated and analyzed with SPSS v.18 using univariable, multivariable, and subgroup analyses.

\textbf{Results and limitations:} Eighty-nine patients were treated with RPN and 78 were treated with R-LESS PN. Baseline characteristics of both groups were similar. Trifecta was achieved in 38 patients (42.7\%) in the multiport RPN group and 20 patients (25.6\%) in the R-LESS PN group (\(p=0.021\)). Patients in the R-LESS PN group had longer mean operative time, warm ischemia time, and increased estimated glomerular filtration rate (eGFR) percentage change. No significant differences were found between the two groups in days of hospitalization, blood loss, postoperative eGFR, positive surgical margins, and surgical complications. Patients with increased PADUA and RENAL scores, infiltration of the collecting system, and renal sinus involvement had an increased probability of not achieving the trifecta. In regression analysis, the type of procedure and the tumor size could predict trifecta accomplishment (\(p=0.019\) and 0.043, respectively). The retrospective study, the low number of series, and the controversial definition of trifecta were the main limitations.

\textbf{Conclusions:} The trifecta was achieved in significantly more patients who underwent multiport RPN than those who underwent R-LESS PN. R-LESS PN could be an alternative option for patients with decreased tumor size, low PADUA and RENAL scores, and without renal sinus or collecting system involvement.

\textbf{Patient summary:} In this study, we looked at the outcomes of patients who had undergone robotic partial nephrectomy. We found that conventional robotic partial nephrectomy is superior to R-LESS partial nephrectomy with regard to the accomplishment of negative margins, reduced warm ischemia time, and minimal surgical complications.

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1. Introduction

Renal cell carcinoma (RCC) represents 2–3% of all cancers [1]. The use of imaging techniques has increased the detection of smaller and lower-stage renal tumors, providing the opportunity to perform nephron-sparing surgery to treat RCC [2]. Robot-assisted, multiport, laparoscopic partial nephrectomy (RPN) is a minimally invasive technique that has gained momentum worldwide for the treatment of small and medium-sized renal masses [3]. With increasing experience in robotic surgeries, there has been a dramatic increase in the adoption of laparoendoscopic single-site (LESS) surgery in urology, since LESS is considered an approach that achieves cosmetic outcomes superior to those of the multiport technique [4–6].

It has been established that positive margins, functional outcomes, and patient safety must remain the surgeon’s top priority in the treatment of a patient having a malignant tumor. Thus, the term trifecta was introduced to estimate multiport RPN success [7]. However, trifecta achievement is not well studied in the R-LESS PN technique. Therefore, we performed a retrospective analysis of our R-LESS PN and multiport RPN series aiming at comparing the possibility of trifecta achievement and the perioperative and postoperative outcomes between these procedures. To our knowledge, no study has been carried out comparing trifecta achievement in the multiport RPN versus R-LESS PN approach.

2. Materials and methods

2.1. Patient selection and outcome measurements

Data from 167 patients with renal tumor who underwent multiport RPN and R-LESS PN by a single surgeon in a tertiary institute between October 2006 and July 2012 were obtained and retrospectively analyzed from our prospectively maintained institutional review board–approved database.

The main outcome measurement was trifecta achievement; secondary outcome measurements were operative time, days of hospitalization (length of stay [LOS]), estimated blood loss (EBL), and postoperative estimated glomerular filtration rate (eGFR) and its percentage change. Based on the published articles regarding trifecta accomplishment and the impact of warm ischemia time (WIT) in renal function, we defined trifecta achievement as a combination of WIT <20 min, negative surgical margins and no surgical complications as a denotation of oncologic and surgical safety, respectively [7–11].

The subjects were stratified into two groups: 89 patients who underwent multiport RPN and 78 patients who underwent R-LESS PN. The patients were sequentially enrolled to RPN or R-LESS PN without any selection criteria.

Preoperative clinical and demographic characteristics (age, sex, body mass index [BMI], tumor location and size, physical status, American Society of Anesthesiologists [ASA] classification, eGFR, and PADUA and RENAL scores) were retrospectively analyzed to identify possible significant differences between the baseline characteristics of these groups. Both PADUA and RENAL scoring systems were used to account for tumor complexity [12,13]. Tumor complexity was stratified as low, moderate, and high if the PADUA and RENAL scores were 6–7, 8–9, and ≥10 and 4–6, 7–9, and 10–12, respectively. We assigned the infiltration of the collecting system using cross-sectional computed tomography images with magnified views, as established in previous studies [12,13]. Perioperative and postoperative outcomes and surgical complications were also analyzed and compared between the groups (operative time, EBL, WIT, postoperative eGFR, number of patients with positive surgical margins, LOS, days of drain maintenance, number of patients who underwent conversion to open surgery, no postoperative complications). To determine the impact of each technique in renal function, we counted and compared the eGFR percentage change between the groups, which was defined as the percentage of difference between preoperative and postoperative eGFR in each group (eGFR change = 1 − (postoperative eGFR / preoperative eGFR) × %).

Patients’ eGFR was determined using the Modification of Diet in Renal Disease Formula [14].

2.2. Surgical technique

The R-LESS PN procedure was performed according to our previously described approach [15]. We used a single-port device consisting of an Alexis wound retractor (Applied Medical, Rancho Santa Margarita, CA, USA) and a size 7 surgical glove. The device was inserted through a 4-cm umbilical incision, while two 8-mm trocars (as robotic arms ports) and two 12-mm trocars (as camera port and assistant port) were introduced through the glove’s fingers (Fig. 1a). During the procedure for right-sided kidney tumors, we decided whether an additional 5-mm port for liver retraction was needed, which was subsequently inserted in the subxiphoid area. The multiport RPN technique was performed using two 12-mm trocars (as camera and assistant port) and three 8-mm trocars (as robotic arms ports). The configuration of trocars in our multiport approach is shown in Figure 1b.

Laparoscopic ultrasound was used intraoperatively in all cases to identify tumor depth and margin. The surgical steps included tumor identification, temporary occlusion of the renal vessels, tumor excision, and renorrhaphy using the sliding clip technique.

2.3. Statistical analysis

Differences between the two groups were compared either by using the independent sample t-test for continuous variables or the chi-square test for 2 × 2 contingency or larger tables. Counts of frequencies were expressed as percentages, and continuous data were presented as the mean plus or minus the standard deviation (SD). WIT was analyzed both as a continuous and categorical (>20 min or <20 min) variable. We performed a subgroup analysis of the multiport and single-site groups to estimate the impact of important variables in the possibility of achieving the trifecta or not. Finally, univariate and multivariate binary logistic regression analyses were performed to determine...
the most important explanatory variables for trifecta accomplishment. For all statistical analyses, a two-sided \( p \) value < 0.05 was considered statistically significant. All analyses were performed using the SPSS statistical package (IBM Corp, Armonk, NY, USA).

### Results

The patients' demographic characteristics are summarized in Table 1. There were not any statistically significant differences in the baseline characteristics between the two groups regarding age (\( p = 0.41 \)), BMI (\( p = 0.40 \)), ASA score (\( p = 0.067 \)), tumor size (\( p = 0.83 \)), PADUA score (\( p = 0.65 \)), RENAL score (\( p = 0.28 \)), renal sinus involvement (\( p = 0.14 \)), and collecting system infiltration (\( p = 0.89 \)).

Table 2 presents the perioperative and postoperative data of both groups. Patients in the R-LESS PN group had longer mean operative time (208 ± 83 min vs 173 ± 75.8 min; \( p = 0.04 \)), longer mean WIT (26.5 ± 10.5 min vs 20.2 ± 12.8 min; \( p = 0.001 \)), and increased mean eGFR percentage change (−21% ± 17.2% vs −14.7% ± 19%; \( p = 0.03 \)) in comparison to multiport subjects. We did not detect any statistically significant differences between the two groups with respect to LOS, EBL, postoperative eGFR, rates of patients with positive surgical margins (1.8% vs 4.8%, respectively), and number of patients with surgical complications (7 vs 4, respectively) (\( p = 0.35 \), 0.65, 0.77, 0.18, 0.18, respectively). In three patients in the multiport RPN group and two in the R-LESS PN group, a conversion to radical nephrectomy was performed due to severe perioperative hemorrhage or difficulties in assessing the tumor extension with the robotic arms. Two patients in the R-LESS PN group required endoscopic ureteral stent placement due to either postoperative urinary leakage or perioperative ureteral injury, and one patient underwent renal artery embolization due to postoperative retroperitoneal bleeding. Seven patients in the R-LESS PN group and four in the multiport RPN group required blood transfusions.

The multiport RPN group had a higher overall trifecta rate than the R-LESS PN group. Trifecta was achieved in 38 patients (42.7%) in the multiport RPN group and 20 patients (25.6%) in the R-LESS PN group, respectively (\( p = 0.021 \)). In univariate analysis, patients with increased tumor size, high PADUA and RENAL scores, infiltration of collecting system, and renal sinus involvement had an increased probability not to accomplish the trifecta (\( p < 0.01 \)).
in all variables). Furthermore, higher blood loss and increased eGFR percentage change were observed in the patients who could not achieve the trifecta (p < 0.01) (Table 3).

By using multiple logistic regression analysis, we determined that the type of procedure (multiport RPN or R-LESS PN) and the tumor size were the only variables that could predict trifecta accomplishment (p = 0.019 and 0.043, respectively) (Table 4).

4. Discussion

Although the trifecta is a well-established concept regarding the efficacy of radical prostatectomy procedures, it is a newly introduced term for the effectiveness of several PN techniques, regardless of the approach used [16]. Like other authors, we believe that the use of a standardized system such as the trifecta must be encouraged by the urologic community, since it can be of ascendant importance to estimate and compare more properly the early efficacy and safety of different nephron-sparing surgical options [10,17,18]. Trifecta assessment has been already studied in the multiport RPN approach and in robotic versus laparoscopic PN cases [7,18]. To our knowledge, the current analysis is the first to compare multiport RPN with R-LESS PN in the era of trifecta accomplishment.

However, the definition of trifecta has not been well established in PN cases yet. Buffi et al described the term margin, ischemia, and complication (MIC)—that is, negative surgical margins, WIT <20 min, and minimal surgical complications—to designate the ideal outcome of patients
undergoing PN [10]. They used the term MIC instead of trifecta because they wanted to avoid confusion with the already introduced trifecta system in prostate cancer surgery. Khalifeh and associates defined trifecta achievement as a combination of negative surgical margins, WIT < 25 min, and no perioperative and early postoperative complications of higher than grade 3 according to the Clavien-Dindo classification system [7], while Hung and colleagues pointed out that three key outcomes of negative cancer margin, minimal renal function decrease, and no urological complications should determine the trifecta actualization [18].

All of these definitions recognize that negative surgical margins and minimal surgical complications are important parameters in trifecta achievement, but controversies still exist as to whether WIT (and how long) or postoperative renal function, as determined by eGFR, should constitute the third variable in trifecta definition. Data from the existing literature suggest that a safe WIT is between 20 and 30 min, although every minute counts when the renal hilum is clamped [11]. On the other hand, Hung et al stated that the percentage of renal function decrease should be the end point [18]. In our statistical analysis, we used a combined definition of negative surgical margins, WIT < 20 min, and no surgical complications, and we distinguished a significant superiority of achieving trifecta in the multiport RPN approach compared to R-LESS PN. But we assume that even if we had chosen to use the proposal of Hung et al for the trifecta concept, the results would have been similar, since we detected that there is a statistically significant increased eGFR percentage change in the R-LESS PN group [18]. Moreover, although we did not find any statistical differences in perioperative and postoperative eGFR between the groups, we did observe a statistically significant eGFR percentage change in the R-LESS PN cases, suggesting that R-LESS PN has a negative impact in early postoperative renal function. The trifecta results in our study are lower compared with previous published studies. This is probably due to the strict definition of trifecta accomplishment used in our analysis. Khalifeh et al reported that 58.7% of multiport RPN procedures achieved trifecta, but the authors considered that the goal of PN was reached when WIT was < 25 min [7]. We analyzed our data using the definition of Khalifeh et al and we found again that multiport PN had superior trifecta outcome compared to the R-LESS PN approach (58.4% vs 37.2%, respectively). But in this case, our results regarding trifecta accomplishment in the conventional approach were similar with those of Khalifeh and colleagues.

Furthermore, we observed that a significantly longer operative time and WIT had occurred in R-LESS PN cases in contrast with the multiport RPN procedure. We also observed that patients with increased tumor size, moderate and high PADUA and RENAL scores, infiltration of the collecting system, and renal sinus involvement had an increased probability for trifecta failure. Correlation of trifecta failure with increasing tumor size has been mentioned by Buffi et al as well [10].

Since the trifecta rate could be influenced by the different anatomic and topographic characteristics of the treated tumor, we also estimated and compared tumor complexity in both groups by PADUA score as well as RENAL score to detect even the smallest differences between the groups. Therefore, we believe that a tumor’s complexity does not constitute a confusing factor in our results. Surgical confounders were minimized using the outcomes of a single surgeon. Moreover, all the procedures were done by a surgeon who was very experienced in robotic surgery, specialized in minimally invasive PN procedures, and had reached the learning curve for both techniques.

Our results seem to be in disagreement with the reports of most of the manuscripts [4,6,15,19,20]. The majority of the published studies stated that R-LESS PN is a feasible procedure performed in an acceptable length of operative time and WIT, resulting in an excellent cosmetic outcome [6,19]. However, the authors of these studies did not include trifecta accomplishment in their analysis. Furthermore, many authors recognize that there are difficulties in performing a R-LESS PN operation, since the current da Vinci system (Intuitive Surgical Inc, Sunnyvale, CA, USA) is not designed to be used in this fashion. The more common problems are instrument conflict (internal or external), significant gas leak, and the insufficient tissue retraction due to the absence of the fourth robotic arm [20]. Other perioperative troubles are the deterioration of instrument mobility in the operative field and the restricted space for the bedside assistant, according to our experience. These difficulties could probably explain the lower trifecta results, the longer operative time and WIT, and, consequently, the increased eGFR percentage change that we found in R-LESS PN cases compared with the multiport approach. Significant improvements in robotic and access platform designs are needed. The recently developed da Vinci single-site surgical platform may resolve these problems, but more studies are needed to estimate the success of this technique [21].

We also identified that in the existing literature there is a lack of comparative studies between the R-LESS PN and multiport RPN techniques. Most of the published studies either compared multiport RPN with laparoscopic PN or they just announced the outcomes of the laparoscopic or R-LESS PN approaches [3,4,6,15,19,20]. Consequently, we believe that because sufficient data are missing, we cannot accept or jump to conclusions regarding the perioperative and postoperative outcomes of R-LESS PN, since this technique is still in its clinical infancy and the advantages of this procedure have not yet been proven. Moreover, we have to consider how clinically meaningful is the superior cosmetic result offered by R-LESS procedure, and have to always bear in mind that the most favorable outcomes that can be achieved following RPN are the triple goals of negative surgical margins, functional preservation, and complication-free recovery, that is, trifecta accomplishment.

There are three limitations to our study. First is the retrospective nature of the study, although data were retrieved from a prospectively maintained institutional database. Second is the low number of patients in both groups. The series is small, but it is reasonable due to the fact that both conventional and R-LESS PN are still innovative
techniques and these results are coming from a single-institution study. The third limitation is the debatable definition of trifecta. Although controversies still exist about the trifecta definition in PN surgery, we tried to overcome this limitation by analyzing both WIT and postoperative renal function.

5. Conclusions

This study has demonstrated that trifecta in RPN is better accomplished by the multiport procedure. The results of our study suggest that the use of the single-site device in R-LESS PN procedures should not be routinely applied in all cases when using the current robotic platform. There will be new types of surgical robotic systems available in the future, so new platforms more dedicated toward single-incision surgery would make R-LESS surgery more readily available for routine urologic use. For the time being, R-LESS PN can be a useful alternative approach in elective patients with small tumor size and low level of complexity, and without renal sinus or collecting system involvement. In case of difficulty in surgery progression, a conversion to reduced port laparoscopy or standard laparoscopy is strongly recommended.

Author contributions: Koon Ho Rha had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Komninos.

Acquisition of data: Komninos, Shin.

Analysis and interpretation of data: Yoon, Koo, Ha.

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