# The learning curve and factors affecting warm ischemia time during robot-assisted partial nephrectomy

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# Abstract

### Introduction:

The learning curve for robotic partial nephrectomy was investigated for an experienced laparoscopic surgeon and factors associated with warm ischemia time (WIT) were assessed.

### Materials and Methods:

Between 2007 and 2014, one surgeon completed 171 procedures. Operative time, blood loss, complications and ischemia time were examined to determine the learning curve. The learning curve was defined as the number of procedures needed to reach the targeted goal for WIT, which most recently was 20 min. Statistical analyses including multivariable regression analysis and matching were performed.

### Results:

Comparing the first 30 to the last 30 patients, mean ischemia time (23.0–15.2 min, $P < 0.01$) decreased while tumor size (2.4–3.4 cm, $P = 0.02$) and nephrometry score (5.9–7.0, $P = 0.02$) increased. Body mass index ($P = 0.87$), age ($P = 0.38$), complication rate ($P = 0.16$), operating time ($P = 0.78$) and estimated blood loss ($P = 0.98$) did not change. Decreases in ischemia time corresponded with revised goals in 2011 and early vascular unclamping with the omission of cortical renorrhaphy in selected patients. A multivariable analysis found nephrometry score, tumor diameter, cortical renorrhaphy and year of surgery to be significant predictors of WIT.

### Conclusions:

Adoption of robotic assistance for a surgeon experienced with laparoscopic surgery was associated with low complication rates even during the initial cases of robot-assisted partial nephrectomy. Ischemia time decreased while no significant changes in blood loss, operating time or complications were seen. The largest decrease in ischemia time was associated with adopting evidence-based goals and new techniques, and was not felt to be related to a learning curve.

**Keywords:** Renal cell carcinoma, partial nephrectomy, robotics

# INTRODUCTION

Over the previous two decades, nephron-sparing surgery (NSS) has become the preferred surgical treatment for T1a and T1b renal masses.[1,2,3] The minimally invasive approach of laparoscopic partial nephrectomy (LPN) combines the benefits of laparoscopic surgery with the benefits of open NSS,[4] resulting in decreased post-operative pain and length of stay in LPN with equivalent oncologic outcomes and post-operative renal function.[5,6,7] However, LPN is a technically challenging procedure with a steep learning curve[8] and a higher post-operative complication rate.[9]

Laparoscopic robot-assisted partial nephrectomy (LRPN) is less challenging than LPN because the robot facilitates precise tumor excision and renal reconstruction with increased degrees of freedom and tremor elimination.[10] Thus, LRPN is increasingly being utilized by surgeons for minimally invasive NSS (Nationwide Inpatient Sample, unpublished data 2007-2012). The goal of our project was to assess the learning curve for LRPN by examining the outcomes of warm ischemia time (WIT), estimated blood loss, complication rates and operating time. Upon defining the learning curve using WIT, we investigated the impact of tumor complexity on the learning curve by matching for RENAL nephrometry scores before and after the learning curve. Furthermore, we analyzed the learning curve with the perspective of our contemporary urologic goals concerning maximum WITs.

# MATERIALS AND METHODS

## Patient selection and surgical technique

Between October 2007 and April 2014, a single surgeon experienced in LPN completed 171 consecutive LRPNs at an academic medical center for T1a and T1b localized renal masses. The surgeon was fellowship trained in endourology with 10 years of post-fellowship clinical experience. Characteristics and perioperative outcomes for these patients were recorded in a prospective database, approved for use by the Institutional Review Board. Initially, reconstruction of the tumor resection site was performed with a running base suture layer followed by a second cortical layer of interrupted sutures.[11] Starting in February 2010, running sutures were used for both the base and the cortical layer.[12] In 14 of 44 (31.8%) procedures completed between July 2013 and April 2014, the second layer of sutures (cortical renorrhaphy) was omitted altogether. Initially, the surgeon's goal was to limit WIT to 30 min. This goal was revised to 20 min within 10 months following the June 2010 publication of results associating damage to renal function with ischemia times over 20 min.[13]

## Complications and renal function

Complications were reported using the Clavien–Dindo classification system with a cut-off of 30 days post-operation for noting post-operative complications. Additionally, we noted the procedures with intra- or post-operative incidences of urine leaks and bleeding. Notably, there were no fatal complications or urine leaks (confirmed post-operatively by examining drain creatinine levels).

Change in renal function was determined using the percent difference in pre- and post-operative glomerular filtration rate (GFR). GFR was calculated using the modification of diet in renal disease 2 (MDRD) equation. Pre-operative GFR was calculated using the most recent creatinine value within 4 weeks preceding the surgery, while the post-operative (nadir) GFR was calculated using the highest creatinine value over the course of the patient's hospital stay. The post-operative follow-up GFR was calculated using the most recent creatinine value between 3 weeks and 18 months following the operation.

## Determination of learning curves and matching

To define the learning curve, the surgical outcomes of estimated blood loss, operative time, WIT and complications were evaluated. WIT was examined on a month-wise basis; surgeries with no warm ischemia were not included in this analysis. The learning curve was defined to be overcome at the first month of surgeries to consistently have a WIT of 20 min or less (our current goal). Following determination of the learning curve, surgeries were matched by RENAL

nephrometry score to account for tumor complexity between cases. After blinding for WIT, surgeries were stratified first by nephrometry score and then by operation date. The cases were matched 1:1 before and after the learning curve; surgeries that could not be matched were removed.

## Statistical analyses

Statistical analyses were conducted with SPSS version 20 (IBM, Armonk, NY, USA) and Stata 13.1 (Stata Corp. LP, College Station, TX, USA). The mean values of characteristics and outcomes were compared using Student's t-test. In comparing complications between two groups (first 30 to last 30; pre- and post-learning curve), a Chi-squared analysis was used. To determine predictors of WIT, a univariate linear regression was used to compare continuous and categorical variables with WIT. A multivariable linear regression was then used to analyze variables found to be independent predictors of WIT on univariate analysis; all variables with a *P* value of 0.05 or less were included in the multivariable model.

# RESULTS

## Patient characteristics and surgical outcomes

The characteristics and outcomes of the LRPN patients were examined [Table 1]. Comparing the first 30 with the 30 most recent operations, there was a marked increase in mean tumor diameter (2.4–3.4 cm, *P* = 0.02) and mean tumor complexity (nephrometry score: 5.9–7.0, *P* = 0.02). Despite this increase in complexity, a significant decrease in WIT (median: 23.0–15.2 min, *P* < 0.01) was observed. All of the remaining characteristics and outcomes remained unchanged or statistically insignificant between the first 30 and the 30 most recent LRPNs, including mean operating room time (206.8–202.9 min, *P* = 78), mean estimated blood loss (EBL) (172.7–171.2 mL, *P* > 0.9), post-operative bleeding (0–2, *P* = 0.16), Clavien grade 3 complications (0–2, *P* = 0.16), Clavien grade 4 complications (1–0, *P* = 0.32), mean body mass index (BMI) (31.7–31.4, *P* = 0.87) and mean age (56.2–59.1, *P* = 0.38). There were no complications with a Clavien grade of 5 in this study [Table 1].

## Determining the learning curve

Next, surgical outcomes as a function of operative date were compared. WIT was determined to be the most informative dependent variable; there were no significant changes in other outcomes, including complication rate, blood loss and total operation time. Thus, WIT was used in defining the learning curve; using the contemporary goal of maintaining WIT at 20 min or less, the learning curve was determined to be overcome after 58 LRPNs [Figure 1]. Two patients were converted to radical nephrectomy in the first 58 cases due to the central or hilar position of the tumor. One patient was converted to open surgery in the first five cases and one case to pure laparoscopic partial in the first 40 cases.

## Investigation and matching for tumor complexity of the patients

Matching based on nephrometry score before and after the learning curve created two groups of 52 patients. Most patient characteristics and outcomes remained the same pre and post-learning curve [Table 2]. Notably, nephrometry score remained the same as it was the matching parameter while WIT exhibited a significant decrease. Figure 2 shows the comparison between WIT and operative date updated for matched nephrometry scores between the pre- and post-learning curve groups.

## Examining Predictors of WIT

Upon examining the characteristics and outcomes that were continuous variables, a univariate analysis revealed that nephrometry score (*P* < 0.001), tumor diameter (*P* < 0.001) and renorrhaphy status (*P* < 0.001) were predictors of WIT [Table 3]. Comparing categorical variables, only the year of surgery was found to be a predictor of WIT (*P* < 0.001). Finally, a multivariable linear regression confirmed that nephrometry score (β = 1.2 min, *P* < 0.001), tumor diameter (β = 1.8 min, *P* < 0.001), cortical renorrhaphy (β = 5.3 min, *P* = 0.004) and year of surgery (β = -1.9 min, *P* < 0.001) were

significant predictors of WIT.

## Comparison of ischemia time with contemporary goals

Comparing WIT with operative date, the surgeries were stratified by the surgeon's goal concerning maximum WIT during the time of operation [Figure 3]. Between 2007 and April 2011, the mean WIT was 25.4 min, while the mean WIT between April 2011 and June 2013 was 19.1 min. For the LRPNs performed between July 2013 and April 2014, cortical renorrhaphy was omitted in 14 (31.8%) patients; the mean WIT during this time was 15.7 min. A single-factor ANOVA found the differences in WITs between these groups to be statistically significant ($P < 0.01$).

# DISCUSSION

In our analysis of a single surgeon's LRPNs, we found that WIT was the only outcome that consistently changed between the first 30 and the last 30 patients. There were no urine leaks or complications with a Clavien score of 5, while differences in the number of Clavien grade 3 and 4 complications and post-operative bleeds remained statistically insignificant. Operating room time, EBL and the remaining outcomes were also similar. Thus, WIT was examined for a learning curve and using the most recent goal of 20 min was found to be 58 cases. All conversions to radical (2), open (1) or pure laparoscopic partial (1) were seen in the first 58 cases. Finally, we matched between pre- and post-learning curve LRPNs based on RENAL nephrometry score. Even after matching, we noticed a significant decrease in WIT, although the other median patient characteristics and surgical outcomes were not statistically different. Finally, we found four predictors of WIT: Nephrometry score, tumor diameter, cortical renorrhaphy and the year the LRPN was performed.

Although the effect of WIT on post-operative renal function is controversial, a WIT of up to 20 min has been our goal since 2011 because of its association with minimal damage to renal function.[14,15,16,17,18,19,20] We defined the learning curve as the number of cases needed to consistently achieve this goal; however, it is notable that prior to 2011, our goal was to limit WIT to 30 min. Our goal was revised in June 2010 based on literature supporting a maximum WIT of 30 min.[13] The changing nature of our goals, reflected in Figure 3, made it difficult for us to examine a learning curve. Between October 2007 and June 2010, of 29 cases, only three had a WIT greater than 30 min, leading us to conclude that the LRPN learning curve for an established laparoscopic surgeon is minimal. Within 10 months of the June 2010 publication, we had adopted and were consistently achieving our new goal of 20 min [Figure 3].

The omission of cortical renorrhaphy resulted in a decrease in WIT from the second half of 2013 onwards [Figure 3]. No urine leaks or bleeding complications were seen when the cortical renorrhaphy was omitted ($n = 14$). By definition, this method utilizes early unclamping, wherein the renal artery is unclamped following the completion of the base layer of sutures at the reconstruction site.[21,22] Previously, the adoption of early unclamping has resulted in decreased WIT. [21,23] However, unlike previously described methods of early unclamping, our method omits cortical renorrhaphy— the second, outer layer of sutures that is otherwise completed following unclamping. We hypothesize that omitting cortical renorrhaphy will improve renal function loss and improve visualization of the base layer to improve access to arterial bleeders. In fact, the %GFR loss improved (-8.1% vs. -2.7%) during the final 30 cases where cortical renorrhaphy was selectively omitted, although this did not reach statistical significance. Interestingly, when looking at the matched cohort [Table 2], despite a significant decline in ischemia time there was no improvement in renal function supporting the principle that resection and reconstruction are important drivers of renal function after partial nephrectomy. A recent matched study showed both improved volume loss (%volume loss: 9 cm$^3$ vs. 17 cm$^3$, $P = 0.003$) and renal function decline (risk of 10% GFR loss: 13% vs 47%, $P = 0.03$) in a group where cortical renorrhaphy was omitted compared with a group with cortical renorrhaphy during partial nephrectomy.[24]

Recent studies have also found minimal learning curves for experienced laparoscopic surgeons adopting LRPN. [11,25,26,27] However, there are some notable differences between our study and the others. First, in comparison with our 171 patients, the four other studies examined between 38 and 50 patients in determining their respective learning curves. Secondly, each of these studies utilized differing definitions of the learning curve. Benway *et al.* found learning curves for the cumulative number of cases needed to reach the absolute minimum operating time (19 cases) and WIT (26 cases).[11] Haseebuddin *et al.* defined the curve as the number of cases needed to reach the point of minimal

variation in operating room time (16 cases) and in WIT (26 cases).[26] Ellison *et al.* calculated their curve as the number of cases needed to reach a plateau in WIT and EBL (33 LRPNs for both), but found no significant decrease in operating room times as the cumulative LRPN number increased.[25] Lavery *et al.* determined the curve as the number of LRPNs needed to reach the average operating time and average WIT of the 18 most recent LPNs (five LRPNs for both variables).[27]

Upon examining our complication rate, we found that we experienced a seamless transition in adopting robotic-assisted partial nephrectomy. Although Gill and colleagues observed a significant complication rate during the adoption of pure LPN, our complication rate was very minimal.[9] However, comparisons to this study are limited as we did not include pure laparoscopic cases in the current study. Our results compare favorably with those of recent studies that also examined the complication rate for robot-assisted partial nephrectomy.[28,29,30]

There are several limitations to our study. First is the retrospective nature of the study. We attempted to minimize selection bias by including all patients who underwent LRPN, although we excluded procedures with no WIT for the purpose of examining the learning curve. Second, not all of the procedures were conducted with the same method for reconstruction. Additionally, we used only one outcome measure, WIT, for determining the learning curve. Finally, our analysis included the LRPNs of only a single surgeon who was experienced in laparoscopic surgery.

Because WIT is an easy variable to track, setting an ideal limit for WIT provided the surgeon a clear goal to strive toward and ultimately accomplish. Based on this association, we hypothesize that creating useful metrics for surgeon feedback can result in changes of surgeon behavior and improved outcomes. We believe that our experience supports the use of evidence-based medicine in urologic practice.

# CONCLUSIONS

For a surgeon who is experienced in laparoscopic partial nephrectomies, adoption of robotic assistance can be performed with a very low complication rate. The ischemia time decreased while no significant changes in blood loss, operating time or complications were seen. The decrease in ischemia time was not felt to be related to a learning curve, but rather to the adoption of stricter goals in 2011, early vascular unclamping and the omission of cortical renorrhaphy from 2013 onwards. Nephrometry score, tumor diameter, cortical renorrhaphy and year of surgery were found to be predictors of WIT on adjusted analysis.

# Footnotes

**Conflict of Interest:** None declared.

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# Figures and Tables

## Table 1



Characteristics and outcomes of the total and the first 30 and the last 30 patients in this study

## Figure 1



Scatter plot of warm ischemia time (WIT) versus operative date for the laparoscopic robot-assisted partial nephrectomies. A linear regression was performed to find a line of best fit. Also on the graph is a line indicating a WIT of 20 min

## Table 2



Comparison of mean outcomes and characteristics between LRPN patients before and after the learning curve using matched data

## Figure 2



Scatter plot of warm ischemia time versus operative date for the laparoscopic robot-assisted partial nephrectomies matched by nephrometry score before and after the learning curve. Surgeries performed after the learning curve are indicated in the shaded box above

## Table 3



Univariable and multivariable linear regression analysis for predictors of warm ischemia time

## Figure 3



Scatter plot of warm ischemia time (WIT) versus operative date for the laparoscopic robot-assisted partial nephrectomies. Surgeries are stratified by goal for maximum WIT (30 min, 20 min, 20 min with omission of cortical renorrhaphy)