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Minimally Invasive Approach in Surgical Management of Renal Neoplasms National Cancer Institute Experience

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Abstract

BACKGROUND: Minimally invasive nephrectomy is considered a technically challenging procedure requiring a long learning curve to reach acceptable warm ischemia time and perioperative complications. These minimally invasive techniques result in a shorter hospital stay and less post-operative pain.

AIM: This study aims to demonstrate the National Cancer Institute experience regarding the benefits of laparoscopic and robot-assisted nephrectomy over open technique.

METHODS: This is a retrospective descriptive cohort study including 62 patients with renal masses treated with nephrectomy whether partial, total or radical, 26 cases were treated by minimally invasive techniques (8 robotic and 18 laparoscopic), while 36 cases were treated by open technique. Inclusion criteria were patients between 20 and 70 years with renal neoplasm without renal vein thrombosis, with tumor stage T1 or T2 N0 M0. Exclusion criteria were patients with medical comorbidities that preclude surgical management or minimally invasive techniques and patients refusing surgery in general.

RESULTS: Minimally invasive nephrectomy resulted in shorter hospital stay (mean hospital stay was 2.2 days for the minimally invasive group and 3.6 days for the open group) and less post-operative pain than open technique ($p < 0.001$ and $= 0.002$, respectively), while open technique resulted in shorter operation time ($p = 0.039$, mean operation time 147.8 min compared to 184.8 in the minimally invasive group).

CONCLUSION: Minimally invasive nephrectomy (laparoscopic and robotic) resulted in less post-operative pain and shorter hospital stay compared to open technique despite consuming longer operation time which may be decreased by improving the learning curve of operating surgeons.

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Introduction

Renal cell carcinoma (RCC) represents 2% of adult malignancies. However, it is the most common malignancy arising in the renal parenchyma [1]. After prostate and bladder cancer, it is the third most common urologic tumor. In the United States, there are approximately 74,000 new cases and almost 15,000 deaths from RCC each year [2].

Laparoscopy and robot-assisted surgery have intervened in all aspects of renal surgery. There is a growing trend to perform fewer and fewer open surgeries on the kidney for renal masses. Furthermore, these minimally invasive techniques are better tolerated by patients, with a shorter hospital stay, and earlier return to normal activity [3].

Objective

This study aims to demonstrate the National Cancer Institute (NCI) experience regarding benefits of laparoscopic and robot-assisted nephrectomy over open technique.

Patients and Methods

This was a retrospective cohort study which included patients presented to the urology unit at NCI; Cairo University with renal tumors (benign or malignant).

The patients were divided into two groups, minimally invasive group including 26 patients (8 robotic

and 18 laparoscopic) and open group including 36 patients. Analysis of patients was done by intention to treat analysis. Patients who were converted from minimally invasive techniques to open technique were included in the minimally invasive techniques group. These cases were treated by surgical intervention between March 2015 and August 2018.

Inclusion criteria were patients between 20 and 70 years with renal neoplasm (benign or malignant) detected by computed tomography (CT) abdomen and pelvis with contrast without renal vein thrombosis, with tumor stage T1 or T2 N0 M0.

Exclusion criteria were patients with medical comorbidities that preclude surgical management or minimally invasive techniques and patients refusing surgery in general.

Patients were diagnosed by history taking and clinical examination in the outpatient clinic and by investigations including laboratory tests (complete blood count, liver function tests, kidney function tests, and coagulation profile) and radiological imaging (CT of abdomen and pelvis with contrast, chest X-ray or CT chest if clinically indicated, with or without bone scan according to symptoms of bone pains or elevated alkaline phosphatase).

Table 1: Fuhrman grading system

Grade	Description
1	Tumors were composed of cells with small (~10 µm) round uniform nuclei with inconspicuous or absent nucleoli
2	Tumor cells had larger (~15 µm) nuclei that exhibited irregularities in the outline and nucleoli when examined under high-power magnification (×400)
3	Tumor cells had even larger nuclei (~20 µm) with an obviously irregular outline and prominent large nucleoli even at low-power magnification (×100)
4	Tumor cells exhibit characteristics similar to those of grade 3 tumors with the addition of bizarre, often multilobed nuclei, and heavy chromatin clumps. These tumors often display areas of spindle-shaped cells resembling sarcomas

Tumor size was measured as the longest diameter of each tumor in any single plane of the pre-operative imaging study. Histological subtyping and pathologic staging were performed according to the 7th edition of American Joint Committee guidelines and cellular grading was performed by the Fuhrman's grading system [4], [5] (Table 1).

Table 2: Clavien–Dindo system

Grade	Definition
Grade I	Any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions Allowed therapeutic regimens are: Drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic, or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications) requiring intermediate care/intensive care unit management
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multorgan dysfunction
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table 2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication

Parameters of evaluation to compare minimally invasive techniques versus open technique included T N M staging, operative factors for both techniques (intraoperative complications, operation time, estimated blood loss, blood transfusion, rate of conversion to open technique), post-operative factors in relation to both procedures (hospital stay, post-operative pain, post-operative complications as bleeding, wound infection, and urine leak), and oncologic safety of the procedure regarding safety margin. Post-operative pain was assessed by pain score (mild, moderate and severe). The early post-operative complications (within 30 days after surgery) were evaluated by central review of medical records for every case included and classified using the Clavien–Dindo system [6] (Table 2).

Statistical analysis

Data were analyzed using IBM SPSS advanced statistics (Statistical Package for Social Sciences), version 24 (SPSS Inc., Chicago, IL). Numerical data were described as median and range or mean and standard deviation as appropriate, while qualitative data were described as frequency and percentage. Chi-square (Fisher's exact) test was used to examine the relation between qualitative variables as appropriate.

A $p \leq 0.05$ was considered statistically significant. All tests were two-tailed.

Results

The clinical and pathological characteristics of all patients are summarized in Table 3.

The mean age was 45 ± 13.4 years for the minimally invasive group and 49 ± 11.9 years for the open group, as shown in Figure 1.

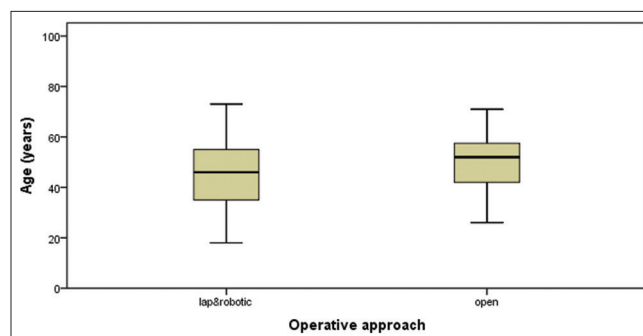


Figure 1: Patients' characteristics regarding age

Sixty cases were diagnosed by CT, while 2 cases by magnetic resonance imaging. Twenty-eight cases had clear cell RCC, 11 cases had papillary

RCC, 12 cases had chromophobe RCC, and 11 cases had other types of pathology. There was no statistical significance regarding pathological staging ($p = 0.193$) and cellular grading ($p = 1$) between the two groups, as shown in Table 3.

Mean operation time was 147.8 min in the open group compared to 184.8 in the minimally invasive group, as shown in Table 4 and Figure 3. Operation time

was shorter in open technique. This was statistically significant ($p = 0.039$).

Mean blood loss during minimally invasive nephrectomy was 383.7 ml compared to 463.3 ml during open technique, but the results were not statistically significant ($p = 0.677$). Mean hospital stay was 2.2 days for the minimally invasive group and 3.6 days for the open group which was statistically significant ($p < 0.001$), as shown in Table 4.

Table 3: Comparison between minimally invasive (laparoscopic and robotic) and open nephrectomy regarding clinicopathological characteristics of the entire patients

Characteristics	Operation approach		Total	p-value
	Lap and robotic (n = 26)	Open (n = 36)		
Post-operative pain				
No				
No	10	2	12	0.001
%	38.5%	5.6%	19.4%	
Yes				
No	16	34	50	
%	61.5%	94.4%	80.6%	
Gender				
Female				
No	17	16	33	0.103
%	65.4%	44.4%	53.2%	
Male				
No	9	20	29	
%	34.6%	55.6%	46.8%	
Need for blood transfusion				
Not needed				
No	23	33	56	0.689
%	88.5%	91.7%	90.3%	
Needed				
No	3	3	6	
%	11.5%	8.3%	9.7%	
Pain degree (n = 50)				
Mild				
No	15 _a	14 _b	29	0.002
%	93.8%	41.2%	58.0%	
Moderate				
No	1	14	15	
%	6.3%	41.2%	30.0%	
Severe				
No	0	6	6	
%	0.0%	17.6%	12.0%	
Tumor size (cm)				
<6				
No	13	14	27	0.357
%	52%	40%	45%	
≥6				
No	12	21	33	
%	48%	60%	55%	
Pathological staging				
PT1a				
No	7	7	14	0.193
%	26.9%	19.4%	22.6%	
PT1b				
No	13	11	24	
%	50%	30.6%	38.7%	
PT2a				
No	4	11	15	
%	15.4%	30.6%	24.2%	
T2bP				
No	2	7	9	
%	7.7%	19.4%	14.5%	
Cellular grading (n = 53)				
Grade 1 and 2				
No	21	27	48	1.000
%	91.3%	90%	91%	
Grade 3 and 4				
No	2	3	5	
%	8.7%	10%	9%	

Open partial nephrectomy (OPN) was converted to radical in 3 cases (due to iatrogenic injury of the left ureter, 1; bleeding from the left renal vein, 1; and bleeding from operative renal bed, 1). Duodenal tear occurred in 1 case in the open group which was treated by primary repair. Laparoscopic nephrectomy was converted to open technique in 6 cases (due to technical difficulty, 2; renal vein bleeding, 1; operative bed bleeding, 2; gonadal vein bleeding, 1). Cases with open conversions were included in the analysis of perioperative complications, as a part of the laparoscopic group with grade IIIb complications.

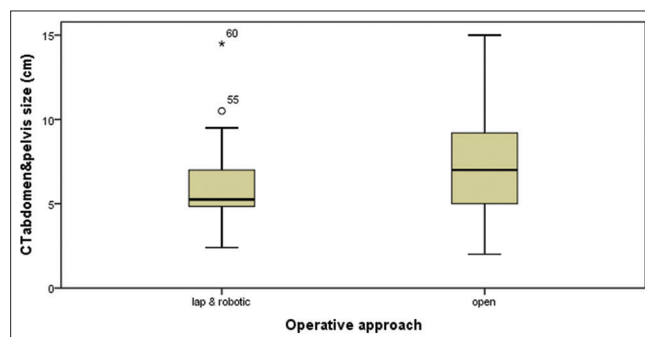


Figure 2: Comparison between minimally invasive (laparoscopic and robotic) and open nephrectomy regarding tumor size

Half of the cases done by minimally invasive technique were located in the lower zone while half of the cases done by open technique were located in the upper zone which was statistically significant ($p = 0.007$). In the laparoscopic group, 4 patients underwent partial nephrectomy, 11 patients underwent total nephrectomy, and 3 patients underwent radical nephrectomy, while in robotic group, 7 patients underwent partial nephrectomy and 1 patient underwent total nephrectomy (Figure 2).

Three patients had positive margin after resection (2 open partial and 1 laparoscopic partial nephrectomies).

Table 4: Comparison between minimally invasive (laparoscopic and robotic) and open nephrectomy regarding age, tumor size, operative time, blood loss, and hospital stay

Operative approach	Lap and robotic (n = 26)					Open (n = 36)					p-value
	Median	Minimum	Maximum	Mean	SD	Median	Minimum	Maximum	Mean	SD	
Age (years)	46.0	18	73	45.2	13.4	52.0	26	71	49.4	11.9	0.204
Tumor size (cm)	5.5	2.4	14.5	6.3	2.6	7	2	15	7.44	3.5	0.170
Operation time (min)	180.0	75	420	184.8	67.0	152.5	45	230	147.8	42.1	0.010
Blood loss	350.0	50	1200	383.7	291.1	300.0	50	2500	463.3	502.4	0.886
WIT (min)	20	15	35	23.45	6.039	22	8	29	20.84	6.362	0.279
Hospital stay (days)	2.0	2.0	3.0	2.2	0.4	3.0	2.00	7.00	3.6	1.1	<0.001

WIT: Warm ischemia time

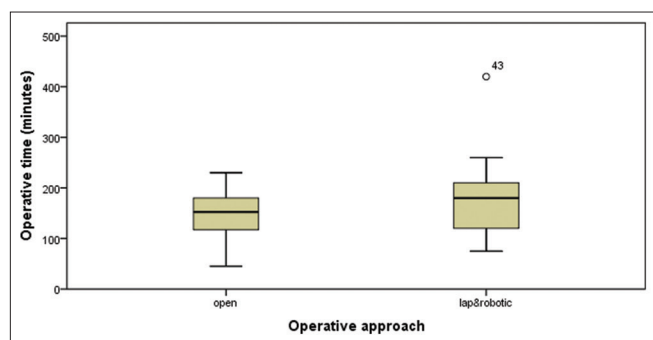


Figure 3: Comparison between minimally invasive (laparoscopic and robotic) and open nephrectomy regarding operation time

Ten patients (38.5%) in the minimally invasive group and 2 patients (5.6%) in the open group did not experience any post-operative pain. Robotic technique was associated with the least post-operative pain which was statistically significant ($p = 0.001$), as shown in Table 5.

Fifteen patients in the minimally invasive group and 14 patients in the open group experienced mild post-operative pain which was statistically significant ($p = 0.002$), as shown in Table 3.

Table 5: Comparison between laparoscopic and robotic nephrectomy regarding post-operative pain (n = 26)

Post-operative pain presence	Operation approach		p-value
	Lap	robotic	
No			0.001
No	3	7	
%	16.7%	87.5%	
Yes			
No	15	1	
%	83.3%	12.5%	

Regarding post-operative complications, 1 patient developed urine leak post-operative after OPN which was treated by image-guided aspiration. Only 1 patient developed wound infection at specimen extraction site after laparoscopic total nephrectomy which was managed by wound culture, antibiotic and frequent dressing. 1 patient developed port site hernia after robotic partial nephrectomy (RPN) which was treated by mesh hernioplasty.

Furthermore, we compared post-operative complication rates between the minimally invasive and open groups and the complication rates were not significantly different between the two groups ($p = 0.147$, as shown in Table 6).

Discussion

In this study, minimally invasive nephrectomy resulted in a shorter hospital stay and less post-operative pain than open technique which was statistically significant, while open technique resulted in shorter operation time which was statistically significant. Another study including 106 patients who underwent

Table 6: Comparison between minimally invasive (laparoscopic and robotic) and open nephrectomy regarding intraoperative and post-operative complications

Complications	Operation approach		Total	p-value
	Laparoscopic and robotic	Open		
Clavien–Dindo classification				
I				0.147
No	1	0	1	
%	3.8%	0.0%	1.6%	
IIIa				1.6%
No	0	1	1	
%	0.0%	2.8%	1.6%	
IIIb				17.7%
No	7	4	11	
%	26.9%	11.1%	17.7%	
No complication				79.0%
No	18	31	49	
%	69.2%	86.1%	79.0%	
Total				100.0%
No	26	36	62	
%	100.0%	100.0%	100.0%	

open, laparoscopic and RPN concluded that RPN offers less blood loss, fewer post-operative complications, and overcomes the technical difficulties of laparoscopic partial nephrectomy (LPN) [7].

Another study including 96 partial nephrectomy patients (54 open, 15 laparoscopic, and 27 robotic) showed that OPN had advantages in operative time and ischemia time, at the expense of increased blood loss, which was, in part, due to differences in operative technique [8].

A separate large series of OPN reported a shorter operation time (155 ± 59 min), but similar ischemia time (20.1 ± 10.9 min) and blood loss (median = 350 mL). A higher (15.3%) transfusion rate was reported [9].

While comparison of RPN to OPN is limited in the literature, there are several studies that compare LPN to OPN. The largest comparison (771 LPN vs. 1,028 OPN) also shows reduced warm ischemia time for OPN versus LPN (30.7 min vs. 20.1 min), positive margins (2.85% LPN vs. 1.6% OPN), and blood loss was similar for OPN and LPN (300 mL vs. 376 mL) with a 5% transfusion rate for both groups [10].

A systematic review and meta-analysis done by Liu *et al.* were published in 2017 comparing laparoscopic radical nephrectomy (LRN) and open radical nephrectomy (ORN) regarding operation time, blood loss, intraoperative complications, hospital stay, time to start oral intake, post-operative complications, and overall mortality. This review included 37 studies, data were available from 14,515 RCC patients, of whom 4844 used LRN and 9671 used ORN for treatment of RCC. Data on intraoperative complications were available for analysis in 695 patients in LRN group with 64 events and 559 patients in ORN group with 48 events. The pooled analysis showed that there was no significant difference in intraoperative complications between LRN group and ORN group. Subgroup analyses showed that LRN group had a significantly higher risk of intraoperative complications than ORN group in patients with mean tumor size smaller than 7 cm [11]. This was similar to our study which showed

that intraoperative complications were more in the laparoscopic group due to lack of surgeons' experience.

In addition, this meta-analysis showed that LRN has been shown to offer superior perioperative results to ORN, including shorter hospital stay, time to start oral intake, and convalescence time, and less estimated blood loss, blood transfusion rate, and anesthetic consumptions but longer operation time [11]. Similarly, our study showed that laparoscopic nephrectomy resulted in longer operation time, less blood loss, shorter hospital stay, less post-operative pain, and shorter time to oral intake than the open technique.

A recent retrospective study done by Lee *et al.* was published in 2018 comparing oncological outcomes and perioperative complications between laparoscopic and open radical nephrectomies in patients with clinical T2 RCC. This study including 964 patients (578 in the open group and 257 in the laparoscopic group) showed that LRN was converted to ORN in 13 cases (because of severe bleeding, 6; other organ damage, 3; and technical difficulty, 4). Furthermore, intraoperative complication rates were not significantly different between the laparoscopic and open groups. This study is the largest among the studies that compared oncological outcomes between ORN and LRN that had a relatively long follow-up period [12]. In our study, 7 patients who were planned for laparoscopic nephrectomy were converted to open technique (2 technical difficulties and 5 bleeding). Similarly, in our study, intraoperative complication rates were not significantly different between the laparoscopic and open groups. In our study, 23 patients had T2 renal masses ≥ 7 cm (7 cases were done laparoscopic and 16 cases done by open technique).

Steinberg *et al.* compared the post-operative outcomes of LRN and those of ORN and found that clinical T2 renal masses can be efficiently managed using the laparoscopic approach, with additional advantages of a shorter hospital stay, decreased blood loss, and more rapid recovery than ORN [13]. Similarly, our study showed that laparoscopic nephrectomy resulted in less blood loss, shorter hospital stay, less post-operative pain, and shorter time to oral intake than open technique.

In another study, Hemal *et al.* also compared post-operative outcomes between LRN and ORN in patients with clinical T2 renal tumors but with a longer follow-up period. They found that the LRN group had superior post-operative outcomes in terms of less blood loss, shorter hospital stay decreased analgesic requirement, and more rapid convalescence even though the LRN group required a longer operation time than the ORN group (180.8 vs. 165.3 min, $p = 0.029$) [14]. Similarly, our study showed that laparoscopic nephrectomy resulted in longer operation time, less blood loss, shorter hospital stay, less post-operative pain, and shorter time to oral intake than open technique.

In a prospective observational comparative study published in 2018 analyzing laparoscopic versus ORN for renal tumors more than 7 cm, thirty patients were included in each ORN and LRN group [15]. In this study, blood loss was more in patients who underwent ORN as compared to those who underwent LRN which was similar to our study. Furthermore, LRN was associated with longer operation time than ORN (187.5 ± 48.49 vs. 163.6 ± 46.35) which was similar to our study which may be due to surgeons' experience which needs to be improved by acquiring more skills and improving learning curve in laparoscopic technique. Longer operation time is associated with slow post-operative recovery due to prolonged anesthesia, but the benefit of less blood loss and less pain usually compensates for better recovery in LRN group despite longer operative times [15].

Furthermore, in this study, mean hospital stay was 6.1 days (range 4–11 days) for patients who underwent ORN and 4.2 days (range 3–8 days) for patients who underwent LRN [15]. Similarly, our study revealed that LRN resulted in shorter hospital stay than ORN which is due to minimal handling of tissues, less post-operative pain, and early oral intake.

The common intraoperative complication in ORN/LRN is vascular injury and bowel injury. In this study done by Khan *et al.*, intraoperative complication rate was similar in ORN and LRN groups. In the ORN group, one patient had inferior vena cava injury due to avulsion of the gonadal vein. One patient in the ORN group had bowel injury (colonic serosal tear). In the LRN group, one patient had bowel injury and one patient had hemorrhage due to clip dislodgement from renal vein [15]. Similarly, in our study, intraoperative complication rates were not significantly different between the laparoscopic and open groups. Laparoscopic nephrectomy was converted to open technique in 6 cases (due to technical difficulty, 2; renal vein bleeding, 1; operative bed bleeding, 2; and gonadal vein bleeding, 1).

Conclusion

Minimally invasive nephrectomy (laparoscopic and robotic) resulted in less post-operative pain and shorter hospital stay compared to open technique despite consuming longer operation time which may be decreased by improving the learning curve of operating surgeons.

Compliance with Ethical Standards

The study was approved by the ethical committee of NCI. Clinical data were collected from

hospital medical records and investigations' reports, recorded in a standard database form, evaluated, and analyzed by the authors. For this type of study (retrospective study), formal consent is not required.

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