Original article

# Complete laparoscopic management of locally recurrent renal cell carcinoma after radical nephrectomy

# Tratamiento laparoscópico completo de carcinoma de células renales localmente recurrente después de una nefrectomía radical

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## Abstract

**Objective:** Description of the laparoscopic approach for local recurrence of renal cell carcinoma after radical nephrectomy and oncological outcomes.

**Study design:** A retrospective cohort analysis.

**Materials and methods:** A retrospective cohort analysis included patients who underwent laparoscopic resection for RCC recurrence at XXX. The laparoscopic technique utilized either transabdominal or retroperitoneal approaches. The primary outcome measure was disease-free survival. Secondary outcome measures included operative time, estimated blood loss, and complications.

**Results:** Thirteen patients underwent laparoscopic resection, with a mean operative time of 189 minutes and low complication rates. Pathological reports confirmed clear-cell RCC in the majority of cases. The median time to recurrence post-nephrectomy was 67 months, with a 3-year disease-free survival rate of 85%. All patients had negative margins, and at the last follow-up all patients were alive.

**Limitations:** The limitations of this study include its small sample size and retrospective design.

**Value:** The full laparoscopic approach for patients with local recurrence of renal cell carcinoma.

**Conclusion:** Laparoscopic resection of locally recurrent RCC post-radical nephrectomy appears to be safe and effective, demonstrating promising oncological outcomes. Larger prospective studies are warranted to validate these findings and establish standardized guidelines for widespread implementation.

**Keywords:** local recurrence of renal cell carcinoma, full laparoscopic approach, oncological outcomes and disease free survival

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## Resumen

**Objetivo**: Descripción del abordaje laparoscópico para la recurrencia local del carcinoma de células renales después de la nefrectomía radical y resultados oncológicos.
**Diseño del estudio**: Análisis de cohorte retrospectivo.
**Materiales y métodos**: Análisis de cohorte retrospectivo que incluyó pacientes que se sometieron a resección laparoscópica por recurrencia de carcinoma renal de células claras en XXX. La técnica laparoscópica utilizó abordajes transabdominales o retroperitoneales. La medida principal que se revise de los resultados fue la supervivencia libre de enfermedad. Las medida secundarias incluyeron tiempo operatorio, pérdida de sangre estimada y complicaciones.
**Resultados**: Trece pacientes se sometieron a resección laparoscópica, con un tiempo operatorio medio de 189 minutos y bajas tasas de complicación. Los informes patológicos confirmaron carcinoma renal de células claras en la mayoría de los casos. El tiempo medio hasta la recurrencia después de la nefrectomía fue de 67 meses, con una tasa de supervivencia libre de enfermedad a 3 años del 85 %. Todos los pacientes tenían márgenes negativos y en el último seguimiento todos los pacientes estaban vivos.
**Limitaciones**: Las limitaciones de este estudio incluyen el tamaño de la muestra y el diseño retrospectivo.
**Valor**: El abordaje laparoscópico completo para pacientes con recurrencia local del carcinoma de células renales.
**Conclusión**: La resección laparoscópica del carcinoma renal de células claras recurrente localmente después de una nefrectomía radical parece ser segura y efectiva, demostrando resultados oncológicos prometedores. Se requieren estudios prospectivos más amplios para validar estos hallazgos y establecer directrices estandarizadas para su implementación generalizada.


**Palabras clave:** recurrencia local del carcinoma de células renales, abordaje laparoscópico completo, resultados oncológicos y supervivencia libre de enfermedad

## Background

In 2020, there were an estimated 431.288 new cases of Renal Cell Carcinomas (RCC) globally,[1] with approximately 5.093 cases reported in Argentina alone.[2] The incidence of new kidney cancers has been steadily increasing since 1990s, although it appears to have leveled off in recent years. Advanced imaging techniques, such as CT scans, have significantly contributed to the detection of previously undiagnosed indolent malignancies.[3] In the USA, it is projected that there will be approximately 81.600 new cases of kidney cancer in 2024 (52.380 men and 29.230 in women), leading to an estimated 14.390 deaths.[3]

The incidence of local recurrence after a radical treatment in patients with RCC is reported

less than 1-2 %.[4–7] There is a debate regarding whether renal fossa recurrence (RFR) represents a *de novo* metastasis or the growth of residual RCC cells.[5] Nonetheless, RFR is widely recognized as a poor prognostic factor and requires appropriate management.

Surgical resection is the standard of care for treating RFR associated with a disease-free survival ranging from 30-62 %.[6,8,9] Despite its efficacy, there are no specific recommendations concerning the surgical approach. Margulis *et al.* (2008) conducted a study on 54 patients who underwent surgical resection for local recurrence. They identified predictive risk factors for cancer-specific survival, including margins, tumor size, sarcomatoid patterns and elevated levels of alkaline phosphatase and lactate dehydrogenase. Notably, 35 % of the patients exhibited no clinical evidence of disease, thereby supporting the utilization of surgical management for this pathology.[4]

The objective of this study is to description the laparoscopic approach for local recurrence of renal cell carcinoma after radical nephrectomy and oncological outcomes.

## Materials & methods

The study was approved by the committee on research ethics at the institution in which the research was conducted and any informed consent from human subjects was obtained as required.

Subjects: A retrospective cohort analysis was performed, including all patients who underwent laparoscopic for renal masses at a single institution between January 2008 and April 2023 with diagnosis of RCC who underwent radical nephrectomy (Table 1). XXX is a tertiary hospital affiliated to XXX specialized in the care of cancer patients. Patients with a pre-operative imaging with a recurrence in the renal fossa without distant metastasis were candidates for surgery.

**Table 1. Primary surgery characteristics**

| Patient | Sex | Age at date of surgery | Ecog status | Surgery approach | Side | Tumor type | Isup | Margin | Tumor size (cm) | Stage |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Male | 52 | 0 | Open-radical | Left | Clear-cell | Iii | Negative | 4,5 | T1bnxmx |
| 2 | Female | 53 | 0 | Open-radical | Left | Clear-cell | Iii | Negative | 5 | T3anxmx |
| 3 | Male | 72 | 0 | Lap-radical | Left | Clear-cell | Iii | Negative | 5 | T1bnxmx |
| 4 | Female | 55 | 0 | Open-radical | Left | Clear-cell | Iii | Negative | 6,5 | T1bnxmx |
| 5 | Male | 79 | 0 | Lap-radical | Right | Clear-cell | Iii | Negative | 5 | T1bnxmx |
| 6 | Male | 75 | 0 | Open-radical | Right | Clear-cell | Ii | Negative | 3,5 | T1anxmx |
| 7 | Male | 79 | 0 | Open-radical | Right | Clear-cell | Ii | Negative | 6 | T1bnxmx |

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|---|---|---|---|---|---|---|---|---|---|---|
| 8 | Male | 69 | 0 | Open-radical | Left | Clear-cell | Ii | Negative | 5 | T1bnxmx |
| 9 | Male | 56 | 0 | Open-radical | Right | Clear-cell | Iii | Negative | 8 | T2anxmx |
| 10 | Male | 48 | 0 | Open-radical | Left | Clear-cell | Ii | Negative | 3,5 | T1bnxmx |
| 11 | Female | 61 | 0 | Open-radical | Left | Clear-cell | Ii | Negative | 5 | T1bnxmx |
| 12 | Male | 59 | 0 | Open-radical | Left | Clear-cell | Iii | Negative | 6 | T1bnxmx |
| 13 | Male | 67 | 0 | Open-radical | Left | Clear-cell | Iii | Negative | 6,5 | T1bnxmx |
| Mean | | 58 | 0 | | | | | | 5,3 | |

All patients underwent a laparoscopic approach, either retroperitoneal or transabdominal. In the transabdominal technique three ports were utilized, with a 12 mm port positioned para-umbilically for the camera, and two additional ports—a 5 mm and a 10 mm—were triangulated with the camera. In certain cases, an additional 5 mm port was employed. The patient is placed in a 45° lateral flank position with the contralateral side down. Full back supports, along with tapes at the level of the pelvis and the chest, are used to secure the torso. The upper leg is extended while the lower leg is flexed with a pillow between the legs.

In the retroperitoneal approach, patients were placed in an opposite lateral flank to the lesion. The operating table was bent to widen the space between the 12th rib and the iliac crest. Unlike the transabdominal approach, the surgeon was placed on the back of the patient. The camara port was placed 2 cm above the iliac crest and in the posterior axillary line. This incision was also used to create the potential cavity space; initially the thoraco-lumbar fascia was perforated followed by digital dissection or balloon assisted. The other two ports were placed for triangulation: a 10 mm port and another 5 mm. details of the resection surgery are presented in Table 2.

**Table 2. Surgical characteristics of RFR**

| Patient | Time to recurrence (months) | Site | Detection Method CT/MRI | Age at date of Surgery | Approach | Tumor size (cm) | Operative time (min) | Estimated blood loss (mL) | Tumor Type | Length of stay (d) | Clavien-Dindo | Follow – Up (months) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | 72 | Right Renal fossa | CT | 58 | Trans | 2,5 | 180 | 300 | Clear-Cell | 2 | | 45 |
| **2** | 21 | Left lumbar node | CT | 55 | Trans | 2 | 180 | 200 | Clear-Cell | 1 | | 65 |
| **3** | 23 | Left renal fossa | CT | 74 | Trans | 1 | 150 | 200 | Clear-Cell | 1 | | 68 |
| **4** | 23 | Psoas muscle node | CT | 57 | Trans | 1 | 180 | 200 | Clear-Cell | 1 | | 12 |
| **5** | 26 | Latero-cava node | CT | 81 | Trans | 4,5 | 240 | 600 | Clear-Cell | 5 | II | 60 |
| **6** | 31 | Latero-aortic | CT | 78 | Trans | 2 | 180 | 400 | Clear-Cell | 2 | I | 36 |
| **7** | 27 | Right Adrenal, epiploon | CT | 82 | Trans | 3 | 150 | 300 | Clear-Cell | 1 | | 26 |
| **8** | 132 | Latero-aortic | CT | 81 | Trans | 1 | 150 | 200 | Clear-Cell | 2 | I | 14 |
| **9** | 8 | Latero-cava | CT | 57 | Retro | 4,5 | 150 | 500 | Inflammatory | 1 | | 14 |
| **10** | 192 | Latero-aortic | CT | 64 | Trans | 2 | 180 | 200 | Clear-Cell | 2 | | 24 |
| **11** | 192 | Left renal fossa | CT | 77 | Retro | 1 | 180 | 200 | Clear-Cell | 1 | | 24 |
| **12** | 72 | Latero-aortic | CT | 75 | Trans | 2,5 | 150 | 300 | Clear-Cell | 1 | | 10 |
| **13** | 48 | Left adrenal | CT | 73 | Retro | 1 | 210 | 300 | Clear-Cell | 2 | | 14 |
| **Mean** | 67 | | | 70 | | 2,2 | 189 | 330 | | 1,7 | | 30 |

To estimate the disease free survival we used the Kaplan-Meier method. The results of the quantitative variables are expressed as mean (and standard deviation) for normally distributed variables or median (and interquartile range –IQR-) for non-normally distributed variables.

## Results

Thirteen patients with a mean age of 58 (range 48-79) underwent full laparoscopic resection of a local fossa recurrence for RCC between 2016-2023. Ten out of the 13 patients were male, while the remaining three were female. Four (31 %) patients received previous o subsequent systemic therapy. The mean operative time was 189 minutes (range 150-240 min) and the estimated blood loss 330 ml. Ten patients were approached transabdominally and three retroperitoneally.

In all cases the local recurrence was removed, with two cases requiring a complementary lymphadenectomy due to histological grade and the partial response to systemic therapy.

Only one patient had a Grade II of the Clavien-Dindo classification of surgical complications, while two had Grade I complications. All patients resumed oral intake on the first post-operative day with a mean hospital stay of 1.7 days (range 1-5 days).

Pathological report revealed CCRC in twelve out of thirteen patients.

In this series the median time to recurrence after nephrectomy is reported as 67 months (5.6 years).

The median follow up duration was 30 months (range 10-68 months). Eleven patients remained free of disease, resulting in a 3-year-disease-free survival (DFS) rate of 85 %. Two patients experienced disease recurrence during the follow up period.

Patient 1 after 12 months of follow up progressed with a lung nodule and a metachronic breast carcinoma, currently under treatment with everolimus. Patient 2, relapsed after 26 months from surgery with a 1 cm ipsilateral right retroperitoneal adenopathy and an 8 mm lung adenopathy currently being treated with pembrolizumab and axitinib.

Two patients received systemic therapy before the surgical resection, with previous biopsy confirmation: the first one, experience a recurrence at 8 months after the radical nephrectomy and was treated with axitinib. After 2 years, she had a persistent left renal fossa lesion measuring 1 cm. Consequently, she underwent a surgical resection with lymphadenectomy, the histological result was inflammatory.

The second one received initially systemic therapy with pazopanib and afterwards bevacizumab due to liver toxicity. After two years of treatment, this patient underwent surgical resection of 1 cm lesion in the renal fossa and a retroperitoneal adenopathy, the histological findings were CCRC.

In one patient, a recurrence was observed in the left adrenal gland and a left iliac lesion at 48 months, the histological finding CCRC and continue with close follow up. After two years, a new finding was identified in the right adrenal gland. Initially, the management decision for this lesion was observation, after changes in size, surgical management was performed, the histological findings CCRC. All patients had negative margins with a short follow up of 12 months.

At the last follow up, all patients included in this study were reported to be alive.

## Discussion

Surgical resection of both initial and subsequent recurrences has demonstrated potential benefit for long-term survival in specific cases.[5] However, there is a lack of well-defined selection criteria for metastasectomy.[7] Previous studies have demonstrated that aggressive surgical treatment of local recurrence, with or without adjuvant therapy, offers the best odds for survival (51 % at 5 years survival) compared to radiation or systemic therapy alone (18 % 5-year survival) or observation (13 % 5-year survival).[8]

The rarity of local RCC recurrences poses challenges in analyzing the benefits of laparoscopy in this context, particularly due to the significant role of selection bias in limited experiences.[7] In this series the median time to recurrence is reported as 67 months (5.6 years), while other studies have reported a median time ranging from of 1.1-3.3 years.[4,5,10–12]

Several series have reported the feasibility of the laparoscopic approach. The trocar placement followed the same pattern as radical nephrectomy, with few complications that were managed laparoscopically as we report in this serie, two patients with Clavien Dindo Classification Grade I and only one patient with Clavien Dindo Classification II. These findings suggest a favorable safety profile for this procedure.

Yohannan and colleagues reports a small series of full laparoscopic approach with a mean operating time of 195 minutes, a length of stay 2.5 days, and an estimate blood loss of 187.5 ml. This technique led to shorter hospitalization time and represented the optimal minimally invasive surgical option to these patients compared to hand-assisted laparoscopic approaches. All patients had negative margins with a short follow up of 12 months. Presently, all patients are alive, and three remain free of disease.[7]

The limitations of this study include its small sample size and retrospective design. Nonetheless, we can conclude that laparoscopic resection of local fossa recurrence for RCC yields favorable results in terms of overall survival and recurrence-free survival. Furthermore, it is noteworthy that perioperative outcomes, blood loss and hospital stay data are favorable.

## Conclusion

The laparoscopic resection of local recurrence in patients with clear-cell Renal Carcinoma subsequent to radical nephrectomy is considered to be safe and reproducible.

However, to fully explore the potential benefits of laparoscopy in this context and establish an international consensus, further large-scale prospective studies are necessary. These studies would contribute to a deeper understanding of the technique`s efficacy and facilitate the development of standardized guidelines for its implementation.

## CRediT Taxonomy

1. Gastón Fernández Candia: **1 –** Conceptualization**;** 3 – Formal analysis; 5 – Investigation; 6 – Methodology; 10 – Supervision; 13 – Writing – Original draft; 14 – Writing - Review and editing.
2. Juan Camean: **2 – Data Curation;** 10 – Supervision; 14 – Writing - Review and editing.

3. Jorge Jaunarena: **2 – Data Curation;** 3 – Formal analysis ; 5 – Investigation; 6 – Methodology; 11 – Validation; 14 – Writing - Review and editing.
4. Joaquin Chemi: **2 – Data Curation;** 5 – Investigation; 10 – Supervision; 11 – Validation; 14 – Writing - Review and editing.
5. Roberto Villalba Bachur: **2 – Data Curation;** 10 – Supervision; 11 – Validation; 14 – Writing - Review and editing.
6. Villoldo Gustavo; **1 –** Conceptualization; **2 – Data Curation;** 6 – Methodology; 10 – Supervision; 11 – Validation; 14 – Writing - Review and editing.

## Conflict of interest

None of the authors have any conflicts of interest or financial ties to disclose.

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