Solitary Metastasis of Renal Cell Carcinoma to the Adrenal Gland - Treatment Outcomes following Laparoscopic Retroperitoneal Adrenalectomy

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Abstract

Objective: The oncological and survival benefits of adrenalectomy in patients with solitary adrenal metastasis following nephrectomy for renal cell carcinoma (RCC) is not known through use of a retroperitoneal laparoscopic technique. This study reports the outcomes of patients who have undergone a laparoscopic retroperitoneal adrenalectomy for a solitary adrenal metastasis from primary renal cell carcinoma.

Materials and Methods: From a prospectively collected single surgeon database of 307 upper tract retroperitoneal laparoscopic cases we identified four patients who underwent laparoscopic retroperitoneal adrenalectomy for solitary RCC metastasis between January 2015 and August 2020. Patient's clinical history, pathology, perioperative and oncological outcomes were reviewed.

Results: The mean age of the patients at initial nephrectomy was 61 +/- 10.8 years and all had negative surgical margins. The median time to diagnosis of adrenal metastasis was 52.6 months (13.6 – 121.0). In three patients, metastasis to the adrenal contralateral to original nephrectomy was identified. All patients underwent a retroperitoneal laparoscopic adrenalectomy, which confirmed metastatic RCC. All surgical margins were clear of disease. Within 90 days post adrenalectomy there was only one Grade 1 Clavien-Dindo complication recorded. One of the patients died with widespread metastatic disease 45 months following his adrenalectomy. The remaining three patients remain cancer free.

Conclusion: Solitary metastatic adrenal recurrence from RCC is rare. This is the largest study identified in the literature that describes a laparoscopic retroperitoneal approach in the removal of solitary adrenal metastatic RCC. This minimally invasive approach can be done safely with low perioperative complications and encouraging oncological outcomes.

Keywords: Renal cell carcinoma, adrenal metastasis, laparoscopic retroperitoneal adrenalectomy, outcomes

Introduction

Renal Cell Carcinoma (RCC) is the 7th most diagnosed malignancy in Australian with approximately 4000 new cases diagnosed each year (1). RCC can be an aggressive cancer in that following curative-intent surgical extirpation up to 1 in 3 patients develop distant metastatic disease (2). Common sites of RCC metastasis include lymph nodes, liver, lung, brain and bones (3). Metastasis to the adrenal glands following a nephrectomy is uncommon and contralateral adrenal metastatic disease is particularly rare. In autopsies undertaken of 400 patients who have undergone a nephrectomy for RCC, only 2.5% of patients were identified to

have metastatic disease in the contralateral adrenal gland (4).

For benign adrenal disorders requiring adrenalectomy laparoscopic surgery is now the gold standard and can be performed via transperitoneal or retroperitoneal approaches (5). An open approach is still advocated for malignant adrenal disease (6). The retroperitoneal laparoscopic approach is a new technique that has potential advantages of lower morbidity compared to both open and transperitoneal procedures. Studies have shown that the retroperitoneal approach, where intraperitoneal organs are avoided, results in reduced operating time, reduced blood loss, superior post-operative pain scores

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and reduced length of stay (6-8). There are limited cases in the literature describing the use of this retroperitoneal approach in performing an adrenalectomy for solitary metastatic RCC in the adrenal gland.

At our centre a laparoscopic fellowship trained urological surgeon, performs on average 27 retroperitoneal laparoscopic upper tract cases per year over the last 11 years and performs laparoscopic adrenalectomy also via a retroperitoneal approach.

Materials and Methods

We reviewed a prospectively collected single surgeon series of retroperitoneal laparoscopic upper tract cases and identified four patients undergoing laparoscopic retroperitoneal adrenalectomy for solitary adrenal metastasis from RCC between 2015 and 2020. Demographic, clinical and histopathological data was retrospectively collected via electronic health records.

Ethics approval was obtained through the Hunter New England Human Research Ethics Committee, in conjunction with Central Coast Local Health District.

Our technique for laparoscopic retroperitoneal adrenalectomy is similar to previous descriptions (9,10). The patient is placed in a lateral decubitus position with the operating table being broken to maximise the distance between the 12th rib and the iliac crest. A four-port retroperitoneal technique is used with an initial 1.5 cm skin incision made below the inferior edge of the tip of the 12th rib, where the muscle and fascial layers are bluntly entered with finger dissection, to create a space for balloon insufflation under vision creating the retroperitoneal working space using a Spacemaker™ Pro Access Dissector System. The balloon is then deflated and then a laparoscope placed. Three

other laparoscopic ports are then placed parallel inferiorly to the 12th rib in line with the primary port site incision (Figure 1). A Medtronic Endo Retractor II 10 mm is used and Gerota's fascia is incised and the perinephric fat is dissected around the adrenal in a "no touch technique" of the adrenal gland. The adrenal vein is double clipped then divided and the adrenal gland is removed with a 10mm Covidien Endocatch bag.

Results

The operative and histopathological features of the primary RCC removed for the patients with subsequent adrenal metastatic disease are summarised in Table 1. Three of the four patients had undergone laparoscopic radical nephrectomy and one patient an open partial nephrectomy. All were pathologically confirmed clear cell RCC with clear surgical margins.

The mean age of the four patients at initial nephrectomy was 61 +/- 10.8 years

The interval from nephrectomy to diagnosis of adrenal metastasis was 52.6 months (13.6-121.0) as outlined in table 2. Three of the four patients were identified to have metastatic disease in the adrenal gland on the contralateral side to their initial nephrectomy.

All four patients were asymptomatic when metastatic disease was identified by routine surveillance CT imaging. Figure 2 displays representative slices the initial radiology of the solitary adrenal tumours identified in the four patients.

All 4 patients underwent a retroperitoneal laparoscopic adrenalectomy. Peri-operative outcomes are described in Table 3. The mean age and BMI of the patients was 70 +/- 6.2 years and 38.3 +/- 4.3 kg/m². The mean operating time was 140 +/- 8.7

Figure 1. Laparoscopic Right Retroperitoneal Adrenalectomy Approach – Four Port Technique. The patient is placed in the lateral decubitus position. The 12th rib and iliac crest are marked prior. The port for the balloon insufflation device which creates the working space in the retroperitoneum is placed 1.5cm below the 12th rib. Two 10mm ports are placed anteriorly and parallel with the iliac crest. These are used for dissection and retraction. A 5mm port is placed posterior to the camera port, in line with the posterior axillary line

Table 1. Histopathology of the primary renal cell carcinoma

Patient	Age	Sex	Year of Operation	Operation	Histopathology	ISUP Grade	Staging (TNM)	Surgical Margins
1	67	M	2016	Left Transperitoneal Laparoscopic Radical Nephrectomy	Clear Cell Renal Cell Carcinoma	3	pT3a, Nx, Mx	Clear
2	75	M	2015	Right Retroperitoneal Laparoscopic Nephrectomy	Clear Cell Renal Cell Carcinoma	3	pT1a, Nx, Mx	Clear
3	55	M	2008	Right Transperitoneal Nephrectomy	Clear Cell Renal Cell Carcinoma	3	pT1b, Nx, Mx	Clear
4	47	M	2002	Left Open Partial Nephrectomy	Clear Cell Renal Cell Carcinoma	3	pT1b, Nx, Mx	Clear

TNM: Tumour, node, metastasis; ISUP: International Society of Urologic Pathologists

Figure 2. Computed Tomography Surveillance revealing solitary adrenal metastatic disease in the four patients, marked in yellow. Time of recurrence and size of the adrenal mass detected was highly variable between patients

Table 2. Detection of disease recurrence from initial nephrectomy

Patient	Time from nephrectomy to identifiable Adrenal Metastasis (Months)	CT Finding
1	15.5	35 mm right contralateral adrenal nodule
2	11.6	29 mm right ipsilateral adrenal nodule
3	89.6	70 mm left contralateral adrenal mass
4	152.3	32 mm right contralateral adrenal mass

CT: Computed tomography

minutes. The mean estimated blood loss was 163 +/- 124.4 mL with no blood transfusions and no open conversions required. The mean hospital length of stay was 2.3 +/- 0.4 days. 3 out of the 4 patients were partly performed by a trainee.

Post-operative complications were classified based on the Clavien-Dindo classification. There was only one recorded complication within the 90-day post-operative period, which

Table 3. Peri-operative outcomes of laparoscopic retroperitoneal adrenalectomy for metastatic RCC

Patient	Side	Age	BMI (kg/m ²)	Operative Time (mins)	Blood Loss (ml)	Length of Stay (days)
1	Right	71	39	155	50	3
2	Right	77	32	135	50	2
3	Left	72	38	135	350	2
4	Right	60	44	135	200	2

BMI: Body mass index

was a Grade 1 complication. This involved superficial wound dehiscence at a laparoscopic port site that required community nursing for wound care. Antibiotics were not prescribed. The wound was inspected two weeks post-operatively and had it healed via secondary intention. No patients were reported to have had endocrine complications as a result of adrenalectomy during this period.

Table 4 lists the pathology of excised adrenal glands. All tumours were consistent with metastatic clear cell RCC, ISUP Grade 3. All surgical margins were clear.

Oncological outcomes are summarised in table 5. At time of writing 3 of the 4 patients are alive and remain disease free. Two patients underwent adjuvant chemotherapy for suspected local recurrence identified on surveillance imaging. One patient died, who developed widespread metastatic disease approximately 20 months post adrenalectomy. This was discovered following a pathological fracture of the right femur. The patient underwent adjuvant chemotherapy and radiotherapy. From time of diagnosis of metastatic disease, the patient survived another 25 months prior to his death. The oncological outcomes of each patient are outlined in Table 5.

Discussion

Solitary adrenal metastatic RCC recurrence post radical nephrectomy in this case series at our institution was rare. This is consistent with published literature. Retroperitoneal

laparoscopic adrenalectomy for solitary adrenal RCC recurrence has not been well described in the literature. While a small series this dataset shows the operation to be safe. Of interest in our case-series the recurrence in three of the four patients was in the contralateral adrenal gland, reflecting the unpredictability of the disease. The underlying pathophysiology of why the RCC spread to the contralateral adrenal gland is not known. It has been proposed it may be due to the rich blood supply of the organ in conjunction with a possibly affinity of the RCC cells for adrenal tissue (11).

The nature of metastatic RCC is variable. Metastatic burden heavily influences survival. Mean survival in patients with heavy metastatic burden is approximately 11 months (12). In patients with solitary metastasis approximately 30% are alive at 5 years (12). The role for local therapy for oligometastatic disease is unclear. Utsumi et al. reporting on surgery for adrenal RCC metastasis achieved a curative outcome in 1 in 3 patients (13).

Where surgical management of solitary adrenal tumours from

Table 4. Histopathological outcomes following laparoscopic retroperitoneal adrenalectomy

Patient	Histopathology	ISUP Grade	Tumour Size (mm)	Surgical Margins
1	Metastatic Clear Cell Renal Cell Carcinoma	3	25x15x22	Clear
2	Metastatic Clear Cell Renal Cell Carcinoma	3	25x25x27	Clear
3	Metastatic Clear Cell Renal Cell Carcinoma	3	60x45x40	Clear
4	Metastatic Clear Cell Renal Cell Carcinoma	3	45x23x13	Clear

ISUP: International society of urologic pathologists

metastatic RCC is advocated, there is no clear evidence in how this should be performed – open or laparoscopic and if minimally invasive: transperitoneal or retroperitoneal. Traditionally open adrenalectomy was recommended for treatment of malignant adrenal lesions. To our knowledge there are no studies comparing retroperitoneal versus transperitoneal laparoscopic surgery in management of solitary adrenal RCC metastasis. Studies of retroperitoneal against transperitoneal laparoscopic renal surgery has shown improved peri-operative outcomes including blood loss, length of stay and post-operative complications (14). This is hypothesised as due to earlier exposure of the critical anatomical structures gained in a retroperitoneal approach, lower risk of injuring intraperitoneal organs plus avoidance of adhesions from previous intra-abdominal surgery.

Several studies have now demonstrated comparable oncological and survival outcomes comparing laparoscopic and open adrenalectomy for patients with adrenal tumours, though not specifically related to the retroperitoneal approach (15,16). A meta-analysis by Jiang et al. (16) comparing transperitoneal laparoscopic adrenalectomy against the retroperitoneal approach in management of pheochromocytoma in 145 patients, found that the retroperitoneal approach was superior (17). Patients who underwent retroperitoneal laparoscopic adrenalectomy were associated with shorter operating times, less intraoperative blood loss and a shorter duration of stay in hospital. There was no difference in post-operative complications between groups (16). Chai et al., performed a systematic review comparing laparoscopic retroperitoneal, laparoscopic intraperitoneal and robotic adrenalectomy for adrenal tumours, but not specifically for solitary adrenal RCC metastasis (17). The review suggested that overall the laparoscopic retroperitoneal approach was superior (17). The peri-operative outcomes in this

Table 5. Oncological outcomes following laparoscopic retroperitoneal adrenalectomy

Patient	Local Disease Recurrence	Distant Disease Recurrence	Adjuvant Chemotherapy or Radiotherapy	Disease Free Survival (Months)	Overall Survival
1	Nil	Nil	No	5	5
2	Nil	Nil	No	35	35
3	Left adrenal mass 43x39x41mm within surgical bed detected 4 months post-operatively. No change in size in four years of surveillance	Nil	Chemotherapy	4	61 months – still alive
4	Nil	Widespread Metastatic Disease - Pathological Fracture of Right Femur, Lytic Lesions T8, T11, Left Scapula, Left Femur, Base of Skull	Chemotherapy & Palliative Radiotherapy	20	45 months

study demonstrate that this technique is associated overall with minimal blood loss, short operating times and length of stay. There are no studies to our knowledge, which have compared the oncological outcomes and survival of patients who have undergone a laparoscopic retroperitoneal adrenalectomy with other approaches. Survival outcomes at 5 years following removal of a solitary adrenal metastasis from RCC has been reported to be between 14–38% (18). A systematic review comparing disease free survival, local recurrence and mortality between laparoscopic and open adrenalectomy for adrenocortical carcinoma found no difference in these outcomes (19).

In spite of rapid advancements in systemic chemotherapeutic therapies for metastatic RCC, long-term disease-free survival for metastatic RCC is rare. Thus, the fact that 3 of the 4 patients treated surgically for oligo metastatic RCC remain recurrence free at the time of this study is promising.

To our knowledge, this is the largest case series of laparoscopic retroperitoneal adrenalectomy for solitary RCC metastasis to the adrenal gland. Our case-series reports perioperative and oncological outcomes over a median follow up of 40 months (20–53). This study shows the technique to be safe and with disease free survival comparable to published literature for other extirpative techniques.

Study Limitations

This retrospective case-series study provides data on a rare clinical scenario managed by a surgical approach not widely utilised. This study does not answer what is the optimal management strategy for solitary RCC metastasis to the adrenal gland. Nor does it provide evidence for this technique over other surgical techniques in those electing for surgical intervention.

However, despite 3 of the cases being performed partly by trainees, the operating time, blood loss, low perioperative complications and length of stay and absence of positive margins suggests this is a reproducible technique even for metastatic disease in the adrenal gland. Ideally larger, prospective randomised studies will need to be undertaken to evaluate and compare this technique against others – transperitoneal, open and robot-assisted; however, these studies are difficult to recruit to prospectively given the rare nature of isolated adrenal RCC metastasis.

Conclusion

We have shown that a laparoscopic retroperitoneal adrenalectomy is a safe operation for the management of solitary adrenal metastatic disease from renal cell carcinoma. While a small series with no control arm, the oncological outcomes are encouraging. Randomised trials are needed to assess the optimal management for solitary RCC metastasis to the adrenal gland and which surgical technique is optimal.

Ethics

Ethics Committee Approval: Ethics approval was obtained through the Hunter New England Human Research Ethics Committee, in conjunction with Central Coast Local Health District.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: C.J.P., M.L.J., Design: C.J.P., M.L.J., Data Collection or Processing: G.A., C.J.P., Analysis or Interpretation: G.A., C.J.P., Literature Search: M.L.J., Writing: C.J.P.

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References

1. Australian Institute of Health and Welfare. Cancer in Australia 2019 (2019). Cancer series no.119. Cat. No. CAN 123. Canberra: AIHW
2. Siegel R., Ward E., Brawley O. & Jemal A. Cancer Statistics. (2011) *CA Cancer J Clin*; 61(4): 212–236
3. Pantuck A., Zisman A. & Belldgrun A. The changing natural history of renal cell carcinoma (2001). *Journal of Urology*; 166(5): 1611–1623
4. Lau W., Zinke H., Lohse C., Chevillat K., Weaver A. & Blute M. Contralateral adrenal metastasis of renal cell carcinoma: treatment, outcome and a review. (2003) *BJU International*, 91: 775–779
5. Ip J., Lee J. & Sidhu S. Laparoscopic Adrenalectomy: The Transperitoneal Approach. (2012) *Current Surgery Reports*; 1: 26–33
6. Mihai R. Open Adrenalectomy. (2019) *Gland Surg*; 8(1): S28–S35
7. Walz MK., Alesina PF., Wenger FA., et al. Posterior retroperitoneoscopic adrenalectomy—results of 560 procedures in 520 patients. (2006) *Surgery*; 140(6):943–50
8. Lee CR., Walz MK., Park S., et al. A comparative study of the transperitoneal and posterior retroperitoneal approaches for laparoscopic adrenalectomy for adrenal tumors. (2012) *Ann Surg Oncol*; 19(8):2629–34.
9. Alesina P. Retroperitoneal adrenalectomy – learning curve, practical tips and tricks, what limits its wider uptake. (2019) *Gland Surg*; 8 (1): S36–S40
10. Chen W., Lin W., Han DJ. & Liang Y. Lateral retroperitoneoscopic adrenalectomy for complicated adrenal tumor larger than 5 centimetres. (2017) *Afr Health Sci*; 17(1): 293–300
11. Sagalowsky A., Kadesjy K., Ewalt D. & Kennedy T. Factors influencing adrenal metastasis in renal cell carcinoma. (1994) *Journal of Urology*; 151(5): 1181–1184
12. Silverman S., Gan Y., Morteale K., Tuncali K. & Cibas E. Renal masses in the adult patient: the role of percutaneous biopsy. (2009) *Radiology*; 240(1): 6–22
13. Utsumi T., Suzuki H., Nakamura K., Kim W., Kamijima S., Awa Y., Araki K., Nihei N., Naya Y. & Ichikawa T. Renal cell carcinoma with a huge solitary metastasis to the contralateral adrenal gland: A case report. (2008) *International Journal of Urology*; 15(12): 1077–1079

14. Hatano K., Horii S., Nakai Y., Nakayama M., Kakimoto K. & Nishimura K. The outcomes of adrenalectomy for solitary adrenal metastasis: A 17-year single-center experience. (2020) *Asia-Pac J Clin Oncol*; 16: e86-e90
15. Sarela A., Murphy I., Coit D. & Conlon K. Metastasis to the adrenal gland: the emerging role of laparoscopic surgery. (2003) *Ann Surg Oncol*; 10: 1191-1196
16. Jiang Y., Qian L., Li Z., Wang KE., Zhou XL., Zhou J. & Ye CH. Comparison of the retroperitoneal versus Transperitoneal laparoscopic Adrenalectomy perioperative outcomes and safety for Pheochromocytoma: a meta-analysis. (2020) *BMC Surgery*; 20 (12); <https://doi.org/10.1186/s12893-020-067604>
17. Chai YJ., Kwon H., Yu HW., Kim SJ., Choi JY., Lee KE. & Youn YK. Systematic Review of Surgical Approaches for Adrenal Tumors: Lateral Transperitoneal versus Posterior Retroperitoneal and Laparoscopic versus Robotic Adrenalectomy. (2014). *International Journal of Endocrinology*; 2014; <https://doi.org/10.1155/2014/918346>
18. Zografos G., Farfaras A., Aggeli C., Kontogeorgos G., Pagoni M., Vogiatzi S., Vasiliadis G. & Papastratis G. Laparoscopic Adrenalectomy for Large Adrenal Metastasis From Contralateral Renal Cell Carcinoma. (2007) *JSLs*; 11(2): 261-265
19. Machado N., Qadhi H., al Wahaibi K. & Rizvi S. Laparoscopic Adrenalectomy for Large Adrenocortical Carcinoma (2015) *JSLs*; 19(3): Machado NO, Al Qadhi H, Al Wahaibi K, Rizvi SG. Laparoscopic Adrenalectomy for Large Adrenocortical Carcinoma. *JSLs*. 2015;19(3):e2015.00036. doi:10.4293/JSLs.2015.00036