

Management of colon-invading renal cell carcinoma: Operative technique and systematic review

Kevin Gerard Byrnes, Jody Sultan Ali Khan, Usman Muhammad Haroon, Niamh McCawley¹, Ijaz Ahmad Cheema

Departments of Urology and ¹Colorectal Surgery, Beaumont Hospital, Dublin, Ireland

Abstract

Invasion into adjacent organs by non-metastatic renal cell carcinoma (RCC) occurs in 1% of patients suitable for resection. Colonic invasion is rare and presents technical challenges. No prospective data exists to guide management of these patients. We present the first reported case of a colon-invading RCC managed with simultaneous open right radical nephrectomy and extended right hemicolectomy. PubMed, Scopus and EMBASE databases were searched for relevant case reports reporting management of colon-invading renal cell carcinoma. Case reports, case series and cohort studies were eligible. A chart review was performed on a patient who presented with right-sided colon-invading RCC. Four previously reported cases were identified. The current case was managed with simultaneous open radical nephrectomy and extended right hemicolectomy. The patient remains well six months postoperatively with no evidence of disease recurrence. Histopathological evaluation of the resected specimen confirmed a T4 clear cell RCC with sarcomatoid differentiation. Colon-invading RCC is rare. This is the first reported case of right-sided, colon-invading RCC treated with radical resection. The current case confirms radical resection is a feasible management strategy for similar presentations. En bloc resection of involved organs remains the only potentially curative option for locally advanced disease.

Keywords: Hemicolectomy, invasive, locally advanced, nephrectomy, renal cell carcinoma

Address for correspondence: Mr. Kevin Gerard Byrnes, MB BCH BAO MCh PhD MRCS, Department of Urology, Beaumont Hospital, Dublin, Ireland.

E-mail: kevingbyrnes@rcsi.com

Received: 03.06.2020, **Accepted:** 12.09.2020, **Published:** 19.01.2021

INTRODUCTION

At detection, 5%–15% of renal cell carcinomas (RCCs) invade into the surrounding structures.^[1,2] Extracapsular spread may involve psoas muscle, pancreas, spleen, small bowel, and colon.^[3-5] Synchronous metastases commonly coexist and preclude surgical intervention. Overall, locally advanced disease confers a poor prognosis, with 5-year overall survival rates of <5%.^[6,7] Nonetheless, *en bloc* resection of involved organs remains the only potentially curative option.

Direct colonic invasion by RCC is rare.^[8,9] Here, we perform a systematic review of the literature to identify previously reported cases of colon-invading RCC. We also outline the operative approach for a recently encountered case of right-sided, colon-invading RCC.

METHODS

Literature search

A systematic review was conducted according to the Preferred Reporting Items for Systematic Review and

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/UA.UA_86_20

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Byrnes KG, Khan JS, Haroon UM, McCawley N, Cheema IA. Management of colon-invading renal cell carcinoma: Operative technique and systematic review. *Urol Ann* 2021;13:1-8.

Meta-Analysis (PRISMA) guidelines.^[10] A study protocol has not been previously published.

Eligibility criteria

All published reports of primary colon-invaing RCC were eligible for inclusion. Case reports, case series, and cohort studies were eligible for inclusion. Conference abstracts were excluded. Eligible studies reported on clinicopathological characteristics, postoperative outcomes, and survival data, where available.

Study outcomes

From the included studies, two reviewers extracted the following details: tumor size, laterality, structures invaied, staging, histopathological features, immunohistochemical features, and surgical management.

Search strategy

Online databases were searched using the following combination of Medical Subject Heading terms: “renal cell carcinoma” OR “RCC” AND “colon.” PubMed, EMBASE, and Scopus databases were searched. The search was performed from inception until May 2020, with the last search performed on May 1, 2020. The titles and abstracts of citations were individually reviewed, and full texts of studies were retrieved, where available. Articles not in the English language were excluded. Reference bibliographies of the recovered studies were further assessed for potential additional publications suitable for inclusion.

Intraoperative photography and chart review

A chart review was performed on a patient who presented with right-sided colon-invaing RCC. The following details were extracted: clinicopathological characteristics, radiological images, intraoperative photographs, histopathological images, operative technique, and postoperative outcomes. Informed written consent was obtained from the patient.

RESULTS

Study selection and characteristics

Figure 1 shows the PRISMA flowchart of our search strategy. The initial search captured 2464 results. After screening, 59 full-text articles were assessed for eligibility. From these, four case reports were identified. One case was identified locally. Following a chart review, five cases of locally advanced T4 RCC invaing the colon were included [Table 1].

Details of previously reported cases

Paine *et al.*^[11] reported the case of a 53-year-old male presenting with intermittent hematochezia and left flank pain. Initial computed tomography (CT) scanning showed

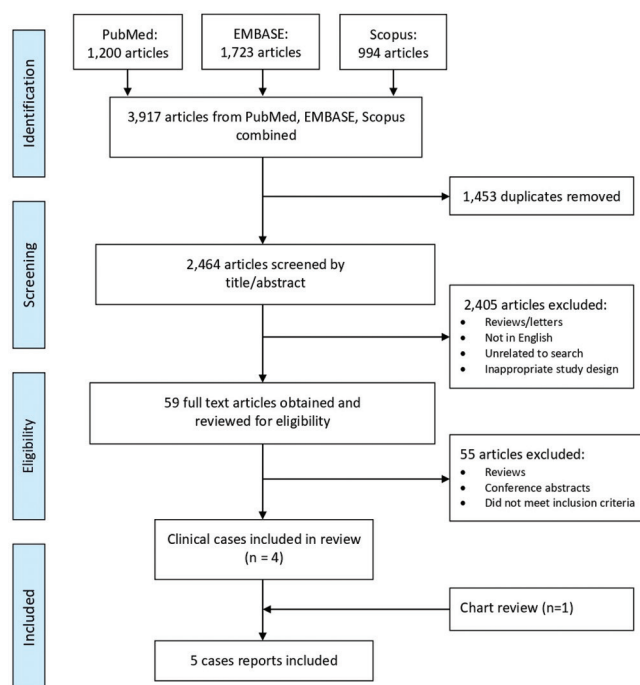


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram of systematic search

a 7-cm left renal mass that was visualized at colonoscopy in the left colon, with fistulous communication present. Biopsy at the time of endoscopy confirmed a poorly differentiated carcinoma, with absence of glandular and squamous features. The authors performed a left radical nephrectomy and partial colectomy with formation of a transverse colostomy. Histopathological evaluation of the specimen showed a mass arising in the renal capsule and invaing the adherent colon. Details on postoperative outcomes were not reported.

Wu *et al.*^[12] reported the case of a 42-year-old male who presented with leg edema, shortness of breath, and weight loss. Due to renal failure, the patient underwent hemodialysis. CT scanning demonstrated a large (28 cm), right-sided renal tumor. Invasion into the caudate lobe of the liver, as well as into the right retroperitoneal structures and the hepatic flexure of the colon, was present. The diagnosis of RCC was confirmed by percutaneous biopsy, which also showed sarcomatoid differentiation. The patient underwent nonoperative management. Survival outcomes were not reported.

Pompa and Carethers^[13] reported a left-sided case of RCC presenting with occult gastrointestinal hemorrhage. CT scanning demonstrated a large (110 mm × 80 mm × 65 mm), left-sided RCC. The mass, in the left lower quadrant, involved the left kidney and descending colon, with extension into the associated adrenal gland and spleen. Biopsy showed a spindle cell RCC, with sarcomatoid

Table 1: Clinicopathological features of reported cases of primary renal cell carcinomas invading into the colon

Authors	Year	Tumor size (mm)	Side	Invading	Stage	Sarcomatoid	Pathology	IHC	Management
Byrnes <i>et al.</i>	2020	51×38×75*	Right	Right colon	pT4	Yes	Clear cell RCC	EMA+, vimentin+, CD10+	Radical nephrectomy and extended right hemicolectomy
Paine <i>et al.</i> ^[11]	2012	112×105×55*	Left	Left colon	pT4	Yes	Clear cell RCC	Keratin+, vimentin+, S100	Left radical nephrectomy and partial colectomy
Wu <i>et al.</i> ^[12]	2007	200×180	Right	Liver, colon, adrenal	pT4	Yes	RCC, unspecified	-	Nonoperative
Pompa and Carethers ^[13]	2002	110×80×65**	Left	Left colon, spleen	pT4	Yes	Spindle cell RCC	-	-
Perez <i>et al.</i> ^[14]	1998	-	Left	Sigmoid colon	pT4	Yes	Clear cell RCC	-	Left radical nephrectomy and left hemicolectomy

*Size from gross pathology specimen, **Size measured by CT. IHC: Immunohistochemical profile, Ki-67 LI: Rabbit anti-human Ki-67 antigen labeling index. EMA: Epithelial membrane antigen, -:Unreported data, RCC: Renal cell carcinoma

differentiated present. Operative management or patient outcomes were not available.

Perez *et al.*^[14] reported a case of left-sided RCC present with lower gastrointestinal hemorrhage. CT scanning showed a left-sided T4 RCC that invaded the left sigmoid colon. This was the first reported case to use colonoscopy-aided biopsy to confirm the diagnosis. Histopathological evaluation showed a clear cell RCC with sarcomatoid differentiation. The authors performed a left radical nephrectomy and left hemicolectomy.

Description of newly reported case

A 68-year-old Caucasian male presented with large-volume melena and collapse. He was hypotensive (80/40 mmHg) on initial assessment and was responsive to fluid resuscitation. Hemoglobin was measured at 11.5 g/dL. There was no history of preceding bowel symptoms, hematuria, or flank pain. Six months previously, he underwent coronary artery stenting and was taking dual antiplatelet therapy. Interestingly, he had a fraternal twin brother who had a nephrectomy for malignancy. A complete urological examination and baseline laboratory investigations were otherwise normal.

A CT scan was performed following identification of the renal mass at focused assessment with sonography for trauma scan. Initial imaging identified a heterogeneously enhancing solid mass in the mid-pole of the right kidney [6.5 cm × 4.3 cm × 5.4 cm; Figure 2]. The tumor extended anteriorly through the Gerota's fascia to involve the posterior aspect of the right colon. There were numerous sub-centimeter paracolic lymph nodes identified on cross-sectional images. However, there was no tumor thrombus seen within the right renal vein, and there was a single right renal artery. Overall, radiological evaluation suggested locally advanced, nonmetastatic RCC. Endoscopic evaluation of the mass showed an exophytic, invasive mass visualized on the posterior intraluminal

aspect of the hepatic flexure of the colon [Figure 3a]. Histopathological evaluation of colonic biopsy confirmed RCC. Following discussion at a multidisciplinary meeting, the patient was planned for simultaneous open extended right hemicolectomy and radical right-sided nephrectomy.

Gross pathological evaluation showed a 5.1 cm × 3.8 cm × 7.5 cm hemorrhagic tumor mass extending through the Gerota's fascia and into the posterior aspect of the right colon. Histopathological appearances confirmed a RCC (clear cell type; ISUP Grade 4) with sarcomatoid differentiation [Figure 3b-d]. Nineteen pericolic nodes were retrieved and were histologically negative for metastatic disease. Final TNM staging was pT4N0M0. The surgical margins were negative. The immunohistochemical profile of the tumor was positive for epithelial membrane antigen, vimentin, and CD10.

On the first postoperative day, he required inotropic support and blood transfusion with two units of packed red blood cells. Ten days postoperatively, the patient developed an ileus. A CT scan showed a small collection (9.8 cm × 8.4 cm) which was amenable to conservative management. He was discharged 15 days following his operation. The patient remains well six months postoperatively with no evidence of recurrence.

Details of operative approach

A transperitoneal approach was used. Access was obtained using a reverse L-shaped incision. This incision extended from the xiphisternum to the umbilicus and then laterally to the right flank. This enabled optimal exposure of right-sided intraperitoneal viscera and retroperitoneal structures.

Mobilization of colic and mesocolic components was performed first, followed by mobilization and *en bloc* resection of the adherent right kidney [Figure 4]. A lateral-to-medial approach was used for mesocolic

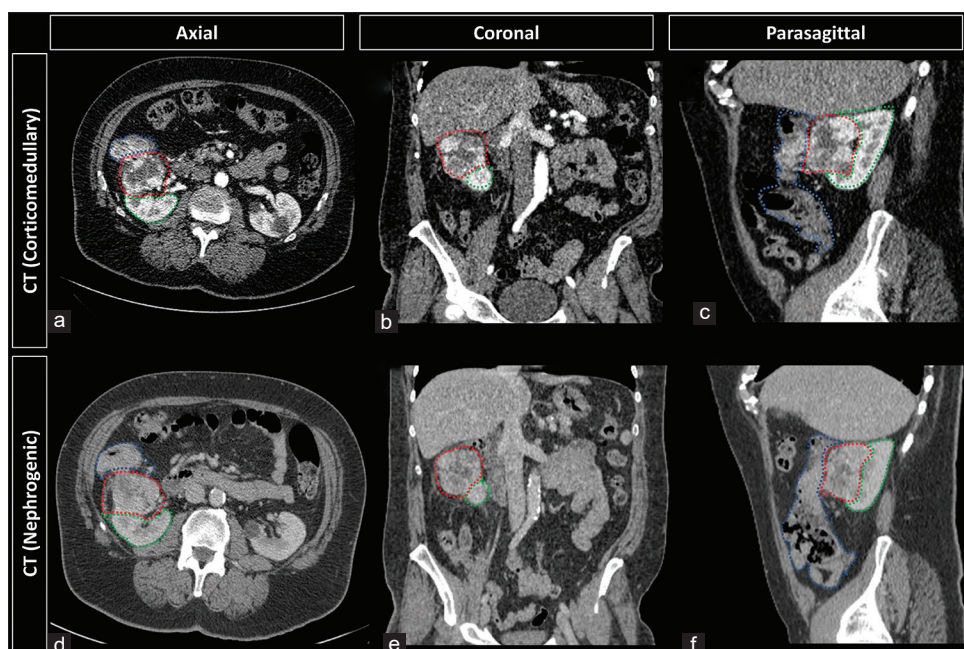


Figure 2: Radiological appearance of renal cell carcinoma invading anteriorly into the right colon. (a-c) Images of axial, coronal, and parasagittal sections from corticomedullary phase of contrast study. Renal cell carcinoma outlined in red dotted line. (d-f) Images of axial, coronal, and parasagittal sections from nephrogenic phase study. Renal cell carcinoma outlined in red, adherent colon in blue, and kidney in green

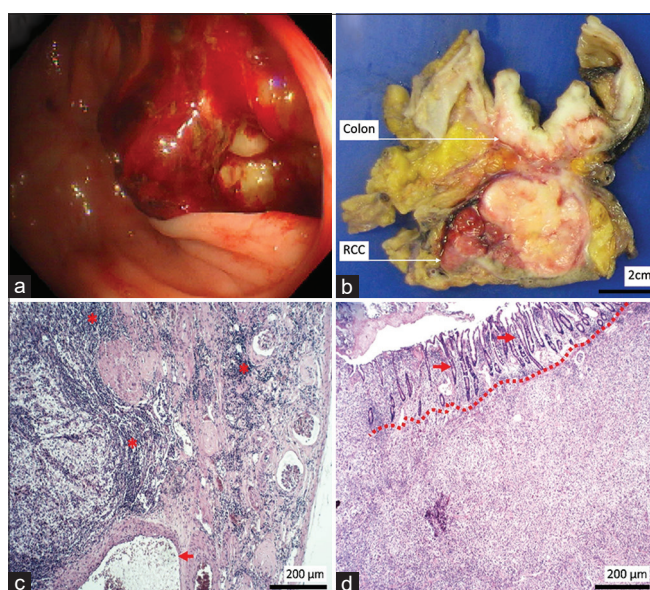


Figure 3: Endoscopic and histopathological appearance of renal cell carcinoma. (a) Photograph taken at colonoscopy demonstrating intraluminal appearance of renal cell carcinoma. (b) Photograph of the postoperative pathological specimen. Axial section at the level of mid-pole of the right kidney demonstrating direct invasion to the right colon. (c) Photomicrograph of axial histopathological section showing severe nephrosclerosis indicated by dense lymphocytic interstitial infiltrate (red asterisk) and glomerulosclerosis. Red arrow indicates a 400 µm deposit of clear cell renal cell carcinoma (ISUP grade 4). (d) Photomicrograph of axial histopathological section of the colon showing preserved colonic mucosa (red arrow) with complete effacement of the submucosa and muscularis mucosa by clear cell renal cell carcinoma (area below red interrupted line)

mobilization, beginning inferior to the tumor. The right paracolic peritoneal reflection was divided and extended

caudad, toward the inferior margin of the right colon. A plane along the Toldt's fascia was further developed using a combination of sharp and blunt dissection. Mobilization was performed cephalad until the inferior margin of the adherent tumor was identified. Separation of the mesofascial plane was extended to the root of the superior mesenteric artery and a high vascular ligation was performed. Ligation of the ileocolic, right colic, and middle colic arteries was performed using nonabsorbable sutures and a LigaSure device (Covidien, Dublin, Ireland). The terminal ileum was divided 10 cm proximal to the ileocecal valve using a linear stapling device. Attention was then turned to mobilization of the colon superior to the tumor. The mid-point of the transverse colon was identified and divided using a linear cutting stapler. Following this, the gastrocolic component of the greater omentum was divided laterally from the line of resection using a LigaSure device.

Mobilization of the colic and mesocolic components enabled their retraction and identification of the underlying structures. These structures included the right renal hilum, duodenum, and inferior vena cava. Dissection of perinephric fat enabled complete mobilization of the right kidney. The kidney and adherent hepatic flexure were retracted inferiorly and anteriorly, enabling access to the posterior aspect of the right renal hilum. Double ligation and sharp division of renal hilar vessels was performed in an artery-first manner using nonabsorbable sutures.

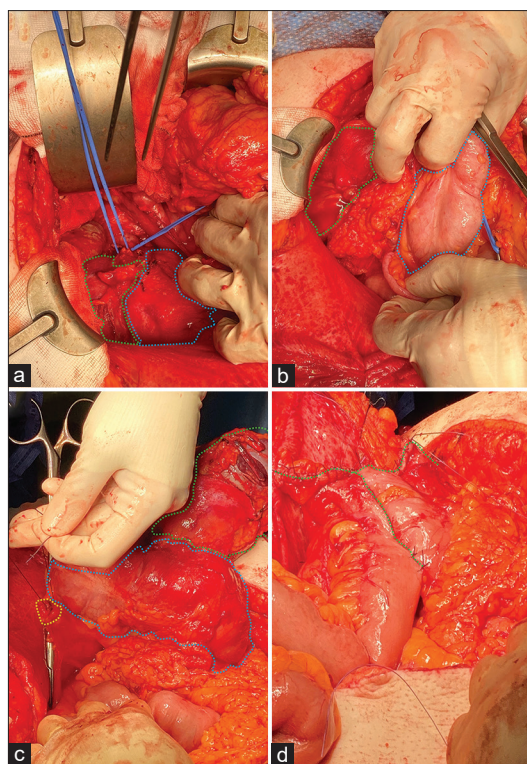


Figure 4: Intraoperative photographs demonstrating simultaneous open radical nephrectomy and extended hemicolectomy. (a) Intraoperative photograph showing identification and exposure of the right kidney (green) and adherent colon (blue) with vascular loops applied to the renal hilum. (b) Intraoperative photograph showing further mobilization of the right colon (blue), mesocolon, and kidney (green). (c) Intraoperative photograph showing fully mobilized kidney (green) and adherent colon (blue) prior to completion of *en bloc* resection. (d) Intraoperative photograph demonstrating side-to-side anastomosis

The gonadal vessels and ureter were ligated, enabling *en bloc* excision of the specimen. A side-to-side ileocolic anastomosis was performed using a linear cutting stapler. Both the terminal ends were sufficiently mobilized to ensure a tension-free and well-vascularized anastomosis.

DISCUSSION

RCC spread occurs lymphatically, hematogenously, transcoelomically, or by direct invasion.^[15-20] Locally aggressive variants are rare. Given the anatomic proximity of the duodenum, numerous authors have reported direct invasion into the duodenal bulb and ampulla.^[9,15,21,22] Gastrointestinal tract invasion may manifest clinically with gastrointestinal hemorrhage or intussusception.^[9,21] However, as the colon and kidney are anatomically remote, direct invasion into the colon is exceptionally rare. A systematic review of the literature found four reported cases of primary RCC invading into the colon [Table 1]. We also present on the reported case successfully managed with open right radical nephrectomy and extended right hemicolectomy.

Colon-invasive RCC typically expresses aggressive histopathological features such as sarcomatoid differentiation. Of the five cases, sarcomatoid differentiation was present in all. Conversely, sarcomatoid differentiation is typically present in <5% of clear cell carcinomas.^[23] Sarcomatoid RCC (sRCC) is characterized by pleomorphic spindle cells and giant cells, producing a sarcoma-like appearance. Due to the locally invasive nature and metastatic potential of sRCC, it heralds a poor prognosis.^[24]

Radical resection of locally advanced tumors is both challenging and controversial.^[3] Clinical trials in oncology are conducted on the principle that tumor invasion to the surrounding structures renders the patient “inoperable.”^[25] No randomized controlled trials are reported on nonmetastatic RCC invading into the adjacent organs. However, large-volume centers, including Memorial Sloan-Kettering Cancer Centre (MSKCC) and MD Anderson Cancer Centre (MDACC), have reported retrospective data on radical resection for locally advanced disease (pT3/T4).^[3] With a median follow-up of 13 months, MSKCC patients incurred a 76% recurrence rate and 90% mortality rate ($n = 36$). Meanwhile, MDACC reported 83% recurrence rate at a median follow-up of 32 months ($n = 30$). Radical resection does not confer substantive survival benefit.^[26] Patients undergoing radical resection therefore need careful counseling on the overall prognosis and risks of surgery.

Despite a lack of data supporting radical resection in terms of overall survival, there is a clear role of *en bloc* resection in locally advanced disease.^[27] With prudent patient selection, improvements in symptoms, quality of life, and palliation are achievable therapeutic goals.^[28-31] Furthermore, pathological involvement of adjacent organs cannot be predicted by preoperative investigations.^[32-36] For example, reactive desmoplasia seen in large RCCs may obliterate fascial planes and mimic pT4 disease.^[37] Tumors are more likely to produce a mass effect through Gerota’s fascia rather than infiltrate it.^[38,39] In locally advanced disease, Margulis *et al.* suggested that 60% of patients are downstaged on histopathological evaluation of specimens.^[3] In the case reported here, we justified radical resection with curative intent on the absence of metastatic disease, the patient’s fitness for surgery, and imminent risk of gastrointestinal hemorrhage.

Careful patient selection relies on anatomical, surgical, and patient factors. Anatomical factors for optimal resection include adequate resection of perinephric adipose tissue, ipsilateral adrenal gland resection, regional lymphadectomy, and an oncologically clear resection of the involved

structures.^[40-47] We opted to perform complete mesocolic excision to achieve an oncologically clear resection, given clinically detectable metastasis disease in the right mesocolon.^[48,49] Failure to obtain a microscopically margin-negative resection is associated with disease progression.^[50-52] For this reason alone, it is important to perform an optimal oncological resection for all the involved structures.

The above factors necessary for optimal oncologic outcomes preclude most patients from resection. However, in patients suitable for radical resection, patient-related factors, such as Eastern Cooperative Oncology Group performance status, lactate dehydrogenase level, serum hemoglobin level, and corrected serum calcium, may aid in the prediction of postoperative morbidity and oncologic outcomes.^[53-55]

Overall, local invasion into the adjacent organs without metastases accounts for <1% of RCC patients suitable for resection.^[3] Currently, no data exist to guide the surgical approach. Laparoscopic and robotic approaches likely have elevated rates of complications due to prolonged anesthesia times.^[56,57] Moreover, laparoscopic management of large tumors is technically demanding. Therefore, an open approach is preferred for locally advanced disease in most cases.^[40,58,59]

Radical resection for locally advanced disease requires careful patient selection and counseling. Simultaneous resection of invaded structures with curative intent is feasible in select patients and can confer added benefits including symptomatic control and improved quality of life.^[60-63] The optimal management of these patients remains unclear. Now that large randomized controlled trials demonstrate the efficacy of targeted therapies including sorafenib and sunitinib in disseminated disease, it remains unclear if surgical intervention and systemic medical therapies can be successfully integrated in select patients.^[64-68]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Lam JS, Belldgrun AS, Pantuck AJ. Long-term outcomes of the surgical management of renal cell carcinoma. *World J Urol* 2006;24:255-66.
- Karellas ME, Jang TL, Kagiwada MA, Kinnaman MD, Jarnagin WR, Russo P. Advanced-stage renal cell carcinoma treated by radical nephrectomy and adjacent organ or structure resection. *BJU Int* 2009;103:160-4.
- Margulis V, Sánchez-Ortiz RF, Tamboli P, Cohen DD, Swanson DA, Wood CG. Renal cell carcinoma clinically involving adjacent organs: Experience with aggressive surgical management. *Cancer* 2007;109:2025-30.
- Hatcher PA, Anderson EE, Paulson DF, Carson CC, Robertson JE. Surgical management and prognosis of renal cell carcinoma invading the vena cava. *J Urol* 1991;145:20-3.
- Sandock DS, Seftel AD, Resnick MI. Adrenal metastases from renal cell carcinoma: Role of ipsilateral adrenalectomy and definition of stage. *Urology* 1997;49:28-31.
- Thompson RH, Chevillie JC, Lohse CM, Webster WS, Zincke H, Kwon ED, *et al.* Reclassification of patients with pT3 and pT4 renal cell carcinoma improves prognostic accuracy. *Cancer* 2005;104:53-60.
- Kavolius JP, Mastorakos DP, Pavlovich C, Russo P, Burt ME, Brady MS. Resection of metastatic renal cell carcinoma. *J Clin Oncol* 1998;16:2261-6.
- Ohmura Y, Ohta T, Doihara H, Shimizu N. Local recurrence of renal cell carcinoma causing massive gastrointestinal bleeding: A report of two patients who underwent surgical resection. *Jpn J Clin Oncol* 2000;30:241-5.
- Sadler GJ, Anderson MR, Moss MS, Wilson PG. Metastases from renal cell carcinoma presenting as gastrointestinal bleeding: Two case reports and a review of the literature. *BMC Gastroenterol* 2007;7:4.
- Moher D, Altman DG, Liberati A, Tetzlaff J. PRISMA statement. *Epidemiology* 2011;22:128.
- Paine E, Daram SR, Bhajee F, Lahr C, Ahmed N, Abell TJ, *et al.* Renal cell carcinoma with direct colonic invasion. *Endoscopy* 2012;44 Suppl 2 UCTN: E82-3.
- Wu MY, Liaw CC, Chen YC, Tian YC, Hsueh S, Jenq CC, *et al.* A giant sarcomatoid renal cell carcinoma. *Nephrol Dial Transplant* 2007;22:952-3.
- Pompa DJ, Carethers JM. Occult gastrointestinal bleeding and colonic mass lesion as initial presentation of renal cell carcinoma. *J Clin Gastroenterol* 2002;35:410-2.
- Perez VM, Huang GJ, Musselman PW, Chung D. Lower gastrointestinal bleeding as the initial presenting symptom of renal cell carcinoma. *Am J Gastroenterol* 1998;93:2293-4.
- Hirota T, Tomida T, Iwasa M, Takahashi K, Kaneda M, Tamaki H. Solitary pancreatic metastasis occurring eight years after nephrectomy for renal cell carcinoma. A case report and surgical review. *Int J Pancreatol* 1996;19:145-53.
- Sountoulides P, Metaxa L, Cindolo L. Atypical presentations and rare metastatic sites of renal cell carcinoma: A review of case reports. *J Med Case Rep* 2011;5:429.
- Johnsen JA, Hellsten S. Lymphatogenous spread of renal cell carcinoma: An autopsy study. *J Urol* 1997;157:450-3.
- Geller JI, Argani P, Adeniran A, Hampton E, De Marzo A, Hicks J, *et al.* Translocation renal cell carcinoma: Lack of negative impact due to lymph node spread. *Cancer* 2008;112:1607-16.
- Stern Padovan R, Perkov D, Smiljanic R, Oberman B, Potocki K. Venous spread of renal cell carcinoma: MDCT. *Abdom Imaging* 2007;32:530-7.
- Ljungberg B, Stenling R, Roos G. Tumor spread and DNA content in human renal cell carcinoma. *Cancer Res* 1988;48:3165-7.
- Cherian SV, Das S, Garcha AS, Gopaluni S, Wright J, Landas SK. Recurrent renal cell cancer presenting as gastrointestinal bleed. *World J Gastrointest Oncol* 2011;3:99-102.
- Faure JP, Tuech JJ, Richer JP, Pessaux P, Arnaud JP, Carretier M. Pancreatic metastasis of renal cell carcinoma: Presentation, treatment and survival. *J Urol* 2001;165:20-2.
- de Peralta-Venturina M, Moch H, Amin M, Tamboli P, Hailemariam S, Mihatsch M, *et al.* Sarcomatoid differentiation in renal cell carcinoma: A study of 101 cases. *Am J Surg Pathol* 2001;25:275-84.

24. Mian BM, Bhadkamkar N, Slaton JW, Pisters PW, Daliani D, Swanson DA, *et al.* Prognostic factors and survival of patients with sarcomatoid renal cell carcinoma. *J Urol* 2002;167:65-70.
25. Bromwich E, Hendry D, Aitchison M. Cyto-reductive nephrectomy: Is it a realistic option in patients with renal cancer? *BJU Int* 2002;89:523-5.
26. Lam JS, Shvarts O, Leppert JT, Pantuck AJ, Figlin RA, Beldegrun AS. Postoperative surveillance protocol for patients with localized and locally advanced renal cell carcinoma based on a validated prognostic nomogram and risk group stratification system. *J Urol* 2005;174:466-72.
27. Kassouf W, Siemens R, Morash C, Lacombe L, Jewett M, Goldenberg L, *et al.* Follow-up guidelines after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma. *Can Urol Assoc J* 2009;3:73-6.
28. Thomas AA, Rini BI, Stephenson AJ, Garcia JA, Fergany A, Krishnamurthi V, *et al.* Surgical resection of renal cell carcinoma after targeted therapy. *J Urol* 2009;182:881-6.
29. Takashi M, Takagi Y, Sakata T, Shimoji T, Miyake K. Surgical treatment of renal cell carcinoma metastases: Prognostic significance. *Int Urol Nephrol* 1995;27:1-8.
30. Swanson DA. Surgery for metastases of renal cell carcinoma. *Scand J Surg* 2004;93:150-5.
31. Maor MH, Frias AE, Oswald MJ. Palliative radiotherapy for brain metastases in renal carcinoma. *Cancer* 1988;62:1912-7.
32. Algaba F, Trias I, Scarpelli M, Boccon-Gibod L, Kirkali Z, Van Poppel H. Handling and pathology reporting of renal tumor specimens. *Eur Urol* 2004;45:437-43.
33. Tay MH, Thamboo TP, Wu FM, Zhaojin C, Choo TB, Ramaan L, *et al.* High R.E.N.A.L. nephrometry scores are associated with pathologic upstaging of clinical T1 renal-cell carcinomas in radical nephrectomy specimens: Implications for nephron-sparing surgery. *J Endourol* 2014;28:1138-42.
34. Weight CJ, Lythgoe C, Unnikrishnan R, Lane BR, Campbell SC, Fergany AF, *et al.* Partial nephrectomy does not compromise survival in patients with pathologic upstaging to pT2/pT3 or high-grade renal tumors compared with radical nephrectomy. *Urology* 2011;77:1142-6.
35. Nayak JG, Patel P, Saarela O, Liu Z, Kapoor A, Finelli A, *et al.* Pathological upstaging of clinical T1 to pathological T3a renal cell carcinoma: A multi-institutional analysis of short-term outcomes. *Urology* 2016;94:154-60.
36. Salmasi A, Faiena I, Lenis AT, Pooli A, Johnson DC, Drakaki A, *et al.* Association between renal mass biopsy and upstaging to perinephric fat involvement in a contemporary cohort of patients with clinical T1a renal cell carcinoma. *Urol Oncol* 2018;36:527.e13-21.
37. Renshaw AA. Subclassification of renal cell neoplasms: An update for the practising pathologist. *Histopathology* 2002;41:283-300.
38. Stecco C, Sfriso MM, Porzionato A, Rambaldo A, Albertin G, Macchi V, *et al.* Microscopic anatomy of the visceral fasciae. *J Anat* 2017;231:121-8. [Doi: 10.1111/joa.12617].
39. Bechtold RE, Zagoria RJ. Imaging approach to staging of renal cell carcinoma. *Urol Clin North Am* 1997;24:507-22.
40. Eggener SE, Yossepowitch O, Pettus JA, Snyder ME, Motzer RJ, Russo P. Renal cell carcinoma recurrence after nephrectomy for localized disease: Predicting survival from time of recurrence. *J Clin Oncol* 2006;24:3101-6.
41. Siemer S, Lehmann J, Kamradt J, Loch T, Remberger K, Humke U, *et al.* Adrenal metastases in 1,635 patients with renal cell carcinoma: Outcome and indication for adrenalectomy. *J Urol* 2004;171:2155-9.
42. Robey EL, Schellhammer PF. The adrenal gland and renal cell carcinoma: Is ipsilateral adrenalectomy a necessary component of radical nephrectomy? *J Urol* 1986;135:453-5.
43. Wunderlich H, Schlichter A, Reichelt O, Zermann DH, Janitzky V, Kosmehl H, *et al.* Real indications for adrenalectomy in renal cell carcinoma. *Eur Urol* 1999;35:272-6.
44. Peters PC, Brown GL. The role of lymphadenectomy in the management of renal cell carcinoma. *Urol Clin North Am* 1980;7:705-9.
45. Giuliani L, Martorana G, Giberti C, Pescatore D, Magnani G. Results of radical nephrectomy with extensive lymphadenectomy for renal cell carcinoma. *J Urol* 1983;130:664-8.
46. Whitson JM, Harris CR, Reese AC, Meng MV. Lymphadenectomy improves survival of patients with renal cell carcinoma and nodal metastases. *J Urol* 2011;185:1615-20.
47. Marshall FF, Powell KC. Lymphadenectomy for renal cell carcinoma: Anatomical and therapeutic considerations. *J Urol* 1982;128:677-81.
48. Hohenberger W, Weber K, Matzel K, Papadopoulos T, Merkel S. Standardized surgery for colonic cancer: Complete mesocolic excision and central ligation-technical notes and outcome. *Colorectal Dis* 2009;11:354-64.
49. West NP, Hohenberger W, Weber K, Perrakis A, Finan PJ, Quirke P. Complete mesocolic excision with central vascular ligation produces an oncologically superior specimen compared with standard surgery for carcinoma of the colon. *J Clin Oncol* 2010;28:272-8.
50. Sutherland SE, Resnick MI, MacLennan GT, Goldman HB. Does the size of the surgical margin in partial nephrectomy for renal cell cancer really matter? *J Urol* 2002;167:61-4.
51. Lam JS, Bergman J, Breda A, Schulam PG. Importance of surgical margins in the management of renal cell carcinoma. *Nat Clin Pract Urol* 2008;5:308-17.
52. Morgan WR, Zincke H. Progression and survival after renal-conserving surgery for renal cell carcinoma: Experience in 104 patients and extended followup. *J Urol* 1990;144:852-7.
53. Park YH, Kim YJ, Kang SH, Kim HH, Byun SS, Lee JY, *et al.* Association between perioperative blood transfusion and oncologic outcomes after curative surgery for renal cell carcinoma. *J Cancer* 2016;7:965-72.
54. Patard JJ, Leray E, Cindolo L, Ficarra V, Rodriguez A, De La Taille A, *et al.* Multi-institutional validation of a symptom based classification for renal cell carcinoma. *J Urol* 2004;172:858-62.
55. Eggener SE, Yossepowitch O, Kundu S, Motzer RJ, Russo P. Risk score and metastasectomy independently impact prognosis of patients with recurrent renal cell carcinoma. *J Urol* 2008;180:873-8.
56. Rabets JC, Kaouk J, Fergany A, Finelli A, Gill IS, Novick AC. Laparoscopic versus open cyto-reductive nephrectomy for metastatic renal cell carcinoma. *Urology* 2004;64:930-4.
57. Mattar K, Finelli A. Expanding the indications for laparoscopic radical nephrectomy. *Curr Opin Urol* 2007;17:88-92.
58. Dunn MD, Portis AJ, Shalhav AL, Elbahnasy AM, Heidorn C, McDougall EM, *et al.* Laparoscopic versus open radical nephrectomy: A 9-year experience. *J Urol* 2000;164:1153-9.
59. Landman J, Olweny E, Sundaram CP, Chen C, Rehman J, Lee DI, *et al.* Prospective comparison of the immunological and stress response following laparoscopic and open surgery for localized renal cell carcinoma. *J Urol* 2004;171:1456-60.
60. MacLennan S, Imamura M, Lapitan MC, Omar MI, Lam TB, Hilvano-Cabungcal AM, *et al.* Systematic review of perioperative and quality-of-life outcomes following surgical management of localised renal cancer. *Eur Urol* 2012;62:1097-117.
61. Clark PE, Schover LR, Uzzo RG, Hafez KS, Rybicki LA, Novick AC. Quality of life and psychological adaptation after surgical treatment for localized renal cell carcinoma: Impact of the amount of remaining renal tissue. *Urology* 2001;57:252-6.
62. Poulakis V, Witzsch U, de Vries R, Moeckel M, Becht E. Quality of life after surgery for localized renal cell carcinoma: Comparison between radical nephrectomy and nephron-sparing surgery. *Urology* 2003;62:814-20.
63. Pannek J, Hallner D, Kugler J, Haupt G, Kruskemper GM, Senge T. Quality of life of patients with renal cell carcinoma or prostate cancer after radical surgery. *Int Urol Nephrol* 1997;29:637-43.
64. Escudier B, Eisen T, Stadler WM, Szczylik C, Oudard S, Siebels M, *et al.* Sorafenib in advanced clear-cell renal-cell carcinoma. *N Engl J Med* 2007;356:125-34.
65. Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM,

- Rixe O, *et al.* Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med* 2007;356:115-24.
66. Motzer RJ, Hutson TE, Cella D, Reeves J, Hawkins R, Guo J, *et al.* Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Engl J Med* 2013;369:722-31.
67. Wood CG. Multimodal approaches in the management of locally advanced and metastatic renal cell carcinoma: Combining surgery and systemic therapies to improve patient outcome. *Clin Cancer Res* 2007;13:697s-702s.
68. Motzer RJ, Rini BI, Bukowski RM, Curti BD, George DJ, Hudes GR, *et al.* Sunitinib in patients with metastatic renal cell carcinoma. *JAMA* 2006;295:2516-24.