

➤ **Original Article** ➤

Surgical Interventions for Renal Cell Carcinoma with Thrombus Extending into the Inferior Vena Cava: A Multidisciplinary Approach

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Objective: To assess surgical strategies and the impact of a multidisciplinary approach on patients undergoing inferior vena caval thrombectomy for renal cell carcinoma and to evaluate perioperative morbidity and mortality associated with these procedures.

Methodology: A retrospective audit for all adults who underwent nephrectomy and inferior vena caval thrombectomy from January 2008 till November 2018 at a University hospital. Patients with incomplete records were excluded from the study.

Results: During the study period, 21 patients underwent inferior vena caval thrombectomy as a completion of radical nephrectomy. Most were males (19:2) with a mean age of 54±11.3 years. The most common surgical approach was the 11th rib flank approach (n=8) followed by midline abdominal (n=6) and Mercedes-Benz (n=5). Eight patients had level 1, 10 patients had level 2, and three patients had level 3 tumour thrombus. The cavotomy was closed primarily in 20 patients; one required inferior vena cava (IVC) reconstruction with a pericardial patch. The proximal clamp was applied below the hepatic veins for most patients. Two patients required suprahepatic clamping before thrombectomy. There was no intraoperative mortality. Five patients (24%) developed complications: two required cardiopulmonary resuscitation due to severe hypotension and were revived; one developed acute renal failure; and one patient

required a damage control laparotomy for excessive oozing. There was no thirty-day mortality.

Conclusion: The IVC thrombectomy, along with radical nephrectomy for renal cell carcinoma for 1–3 level thrombus, can be performed with acceptable morbidity in a multidisciplinary team approach.

Keywords: carcinoma, renal cell, vena cava, inferior, thrombosis

Introduction

In about 4% to 19% of patients with renal cell carcinomas (RCCs), tumours extend into the inferior vena cava (IVC).¹ IVC thrombus in RCC patients has a significant adverse impact on the overall prognosis. Surgical extirpation of both renal tumour and IVC is the standard treatment option. Performing tumour thrombectomy in the IVC is associated with better outcomes in this subgroup of patients.² Since there are few alternative management options, like systemic therapy and radiotherapy, aggressive surgical removal of the tumour and thrombus remains the primary option for patients.^{3,4} Current evidence does not associate a higher level of thrombus with accelerated tumour dissemination to lymphatics in the perinephric fat or distantly. Preoperative embolization is associated with increased morbidity,⁵ and use of IVC filters remains uncertain. The best approach for surgical treatment of these patients remains unclear. The study objectives are to assess surgical strategies for patients undergoing IVC thrombectomy for renal cell carcinoma with thrombus extending into the IVC and to evaluate associated perioperative morbidity and mortality.


Methodology

We conducted a retrospective audit of adult patients (>18 years) who underwent tumour nephrectomy and IVC tumour removal at a University hospital from January 2008 through November 2018. The Institutional Review Board granted an exemption for this study (2018-0583-568). All

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patients had surgery performed under general anesthesia.

Computed tomography (CT) of the abdomen was performed before surgery, and the tumours were classified into four categories, according to the cranial extension of the thrombus into the IVC, as described by Neves and Zincke.⁶⁾ The patients were approached through midline, subcostal, chevron or Mercedes-Benz incisions, depending on patient habitus, tumour size, tumour thrombus level, and surgeon experience. The specific surgical technique was selected on the thrombus extension level. This also guided the surgical approach and teams to be involved. We had excellent communication with anesthesia and the blood bank teams. For level 1 and 2 tumour thrombus, both the urology and vascular surgery teams usually work in tandem for minimal IVC handling until the proximal extent is defined and controlled. For a level 1 tumour, a cavotomy was performed and the tumour removed after control of the proximal and distal vena cava and contralateral renal vein. If the tumour were limited to the renal vein, a tumour thrombectomy was performed, with little dissection, after applying only a side-biting clamp. Primary repair was performed if there were no significant vein defect; if there were, patch repair was considered. For a level 2 tumour, IVC control above the thrombus was more difficult; it required hepatic mobilization in case of retrohepatic extension. After getting control of the infra-renal IVC, contralateral renal vein, and supra renal IVC, the tumour thrombus was removed en bloc if possible. For level 3 tumours, the hepatic surgery team was involved. The same control was achieved, but the proximal clamp was applied to the suprahepatic area. The patient was placed in the reverse Trendelenburg position. The liver was rolled to the patient's left, and the IVC was opened along the anterolateral aspect to the level of the hepatic veins. After complete hepatic mobilization, the supra hepatic IVC, infra renal IVC, contralateral renal vein, and hepatoduodenal ligaments were occluded sequentially to perform the thrombectomy in a bloodless field. The surgical team would then complete the nephrectomy and remove the specimen. The thrombus was removed en bloc through longitudinal cavotomy, but in some instances, it adhered to the wall and was removed piecemeal. Every effort was made to ensure there was no residual thrombus in the proximal portion by back bleeding before final closure of the cavotomy. To prevent air embolism, the patient was placed in a Trendelenburg position for back bleeding from the proximal end.

Patients with incomplete follow-up or incomplete records were excluded from the study. All the data were collected retrospectively from patients' medical records on specially designed proforma. The data included patient demographics, comorbidities, tumour thrombus levels, incision for exposure, surgical strategy use, total blood loss

(ml), total operative time (h), intensive care unit (ICU) stay (days), total hospital stay (days), perioperative morbidity and mortality.

The data was analyzed on SPSS version 20.0 (IBM Corp., Chicago, IL, USA). Descriptive statistics were reported for the quantitative variable as mean \pm standard deviation (SD)/Median (interquartile range [IQR]) and for categorical variables was reported as frequency (%).

The outcome measures were mortality (intraoperative or within 30 days postoperatively), morbidity, ICU stay, and blood loss.

Results

During the study period, 21 patients underwent IVC thrombectomy to complete the radical nephrectomy (Table 1). Most were males (19:2) with a mean age of 54 (SD \pm 11.3) years. The most common surgical approach was the 11th rib retroperitoneal/extra pleural approach (n=8) followed by midline (n=6) and Mercedes-Benz (n=5). Eight patients had a level 1, 10 patients had a level 2, and three patients had a level 3 tumour extension. No patients had tumour extension into the right atrium. The most common procedure was radical nephrectomy and IVC thrombectomy with primary closure. In one patient, IVC was reconstructed with a pericardial patch (Table 1).

Table 1 Basic demographic data, surgical approaches employed, IVC closure technique and vascular control technique

n=21	
Mean age (years) (\pm SD)	54.8 (\pm 11.3)
Gender (male : female)	19 : 2
Side of tumour (right : left)	18 : 3
Level of tumour thrombus	
Level 1	8 (35%)
Level 2	10 (50%)
Level 3	3 (15%)
Level 4	0 (0%)
Surgical approaches	
Midline	6 (30%)
Subcostal	8 (35%)
Mercedes-Benz	5 (25%)
Thoracoabdominal	1 (5%)
Chevron	1 (5%)
IVC reconstruction	
Primary closure	20 (95%)
Patch closure of IVC	1 (5%)
Level of proximal clamping	
a. Sub hepatic	14 (70%)
b. Retro hepatic below hepatic veins	4 (20%)
c. Supra hepatic	2 (10%)

IVC: inferior vena cava; SD: standard deviation

Distant metastasis was identified in four patients preoperatively. The proximal clamp was placed below the hepatic veins except for two patients who required suprahepatic clamping before thrombectomy (Table 1). Nephrectomy was performed first with ligation and division of the renal artery and vein; the kidney was removed for better access. After exposure and clamping of the IVC, the tumour thrombi were removed through an anterior cavotomy. The mean operative blood loss was 2,893 ml (\pm 2,447). The mean operative time was 4.5 h (Table 2). There was no intraoperative mortality. Two patients required cardio-

pulmonary resuscitation (CPR) due to severe hypotension and were revived. One patient developed acute kidney injury; however, it resolved with conservative treatment. One patient with a relatively larger renal tumour developed hypothermia and coagulopathy at the end of the operation. There was excessive oozing from the dissection bed. The patient required a damage control laparotomy and the abdomen was closed after 48 h (Table 2). Most of the tumour thrombectomies were accomplished via the 11th rib approach, which was common for level 1 tumour thrombus, while the Mercedes-Benz was used for level 3 tumours (P-value = 0.02) (Table 3).

More blood loss tended to occur with increased tumour thrombus levels. Higher tumour thrombus levels were also associated with longer operation times (Table 4).

Table 2 Outcome variables showing total blood loss, mean operative time (from incision to wound closure), total hospital stay, ICU stay and different complications

Variables n=21	
Total estimated blood loss (ml) (\pm SD)	2893 (\pm 2447)
Total operative time (h) (\pm SD)	4.7 (\pm 1.4)
Total hospital stay (days) (\pm SD)	8.3 (\pm 3.61)
Mean ICU stay (days)	4.5
Perioperative complications	
Pulmonary embolism	1
Acute renal failure	1
Severe intraoperative hypotension (requiring CPR)	2
Severe hypothermia	1
30-day mortality	0

ICU: intensive care unit; SD: standard deviation; CPR: cardio-pulmonary resuscitation

Discussion

The American Cancer Society's most recent estimates for kidney cancer in the United States indicate there were nearly 63,340 new cases of kidney cancer (42,680 in men and 22,660 in women) in 2018. Approximately 14,970 people (10,010 men and 4,960 women) will die from this disease.⁷⁾ RCC has a biological predisposition for direct vascular invasion. Intravascular tumour thrombus is found in 10%–40% of patients with RCC in the renal vein or IVC.⁸⁾ IVC thrombus is a poor prognostic indicator, with a life expectancy of less than six months in untreated cases.⁹⁾ A radical nephrectomy and cava throm-

Table 3 Different surgical approaches, proximal clamping, perioperative complications, and ICU stay between different thrombus levels

Variables	Level 1 (n=8)	Level 2 (n=10)	Level 3 (n=3)	P-value
Male	8 (100%)	8 (80%)	3 (100%)	0.632
Right sided of tumour	7 (100%)	8 (80%)	3 (100%)	0.632
Surgical approaches				0.022
a. Subcostal	7 (90%)	1 (10%)	0 (0.0%)	
b. Mercedes-Benz	0 (0.0%)	3 (30%)	2 (66.7%)	
Suprahepatic clamping	0 (0.0%)	0 (0.0%)	2 (66.7%)	0.016
Perioperative complications	1 (14.3%)	1 (10%)	2 (66.6%)	0.06
ICU stay (days)	0 (0.0%)	3 (30%)	3 (99.9%)	0.03
T3 N0 Mx	5 (71.4%)	7 (70%)	1 (33.3%)	0.355

ICU: intensive care unit

Table 4 Differences in total blood loss (ml), total operative time (h) and total hospital stay (days) between different levels of tumour thrombus

	Level 1 (n=3)	Level 2 (n=10)	Level 3 (n=3)	P-value
Total EBL (median) (IQR)	1,000 (670–1,800)	2,250 (1,500–6,250)	4,000 (1,500–4,000)	0.07
Total operative time (h) (median) (IQR)	3.75 (3.00–5.00)	5.25 (4.37–6.00)	5.50 (4.1–5.00)	0.134
Total hospital stay (days) (median) (IQR)	6 (5.00–7.00)	8 (6.5–12.00)	10 (7.00–10.00)	0.055

EBL: estimated blood loss; IQR: interquartile range

nectomy is one of the most potent management strategies associated with long-term survival. Radical extirpative surgery, with nephrectomy and IVC thrombectomy, only provides medium term survival.¹⁰⁾ In a recently reported large series, Master et al.¹¹⁾ noted that resection of RCC with IVC tumour thrombus yields long-term survival. Haferkamp et al.¹²⁾ noted that patients with metastatic disease, IVC thrombus, and RCC have better survival with surgical extirpation followed by tyrosine kinase inhibitors (TKI). For RCC patients without distal metastases who undergo radical nephrectomy and IVC tumour thrombectomy, the five-year survival rate has been reported to be 45%–69%.¹³⁾ Temporary filters and liver mobilization techniques improve the safety and prognosis of radical nephrectomy and IVC thrombectomy in renal cell carcinoma with subdiaphragmatic thrombosis.

Berg was the first to report nephrectomy and cavotomy to treat RCC with tumour thrombus extending into the IVC.¹⁴⁾ Since Berg's first report, radical nephrectomy with vena cavotomy has become a safe and effective treatment for RCC with IVC thrombus. The 30-day mortality for radical nephrectomy with IVC thrombectomy has been reported to be 1.5%–10%, and the complication rates have been reported to be 18%, 20%, 26%, and 47% for IVC tumour thrombus level I, II, III, and IV disease, respectively.¹⁵⁾ Fortunately there was no 30-day mortality in our series. The complication rate is 30%, which is comparable to the contemporary series. We consider this to our multidisciplinary approach. Most of the patients with level 1 were approached through flank or subcostal incision. This depended on the individual tumour size and the surgeon choice. If the tumour thrombus was higher, wider incisions were used. More patients were approached via Mercedes-Benz or chevron incisions. The wider exposure did help complete this radical procedure safely. Although level 1 tumours do not require any complex maneuvers, except for control of the IVC above and below the tumour, level 2 and 3 tumours require more complex maneuvers. There was a patient in with level 1 who had catastrophic bleeding while undergoing dissection around the renal vein. He ended up in acute renal failure. This highlights the practical difficulty while dissecting around these tumours when the natural planes are lost, tissues are thick, and the hyperemic anatomy is distorted. Getting adequate exposure was always helpful.

One of the challenges is managing these patients' hemodynamic disturbances as they undergo thrombectomies. Whereas temporary occlusion of the infrahepatic IVC can be safely be done for level 1 tumours, the occlusion of the suprahepatic IVC often causes a profound decrease in venous return, resulting in hypotension. Before applying clamps, patients were well hydrated and were hemodynamically stabilized. There was also a check of clamping,

for a minute, for hemodynamic disturbances before proceeding to cavotomy. There are various ways, described during IVC thrombectomy and nephrectomy, to prevent intraoperative hypotensive shock and pulmonary embolism. These include veno-venous bypass, cardiopulmonary bypass, and deep hypothermic circulatory arrest. However, there are alternate ways to control vessels, including IVC and hepatic pedicle suffices. In a recent report Chen et al.¹⁶⁾ showed the safety of treating level III IVC, concomitant to RCC, by precisely controlling IVC and hepatic vessels without a vascular bypass.

Two patients had severe hypotension after proximal clamp application, but were revived with brief cardiopulmonary resuscitation. The various strategies mentioned in literature to deal with these hemodynamic changes, from proximal clamping as veno-venous bypass, were backup strategies for our patients. None of them required it. We retrospectively think that using these strategies proactively would have avoided these hemodynamic changes.

Renal tumours often invade the vena cava wall, regardless of thrombus level.¹⁷⁾ One patient with this invasion required IVC reconstruction with a pericardial patch.

The median blood loss in this case series ranges from 1,000 ml for level 1 to 4,000 ml for level 3. This signifies need to continuously resuscitate these patients intraoperatively. We also employed damage-controlled strategies when needed in an occasional patient. As mentioned, one patient had level 2 thrombi. During dissection for the nephrectomy and thrombectomy, the patient experienced oozing and was on the verge of becoming hypothermic at the end of operation. It was decided to temporarily pack the abdomen and resuscitate the patient in the ICU. The patient was revived and returned to the operating room after 48 h for removal of packs and definitive closure of the abdomen.

One of our patients had a pulmonary embolus that was not present before surgery. The embolus was suspected on a routine postoperative chest X-ray and subsequently confirmed on chest CT. Indeed, pulmonary metastases from IVC thrombus are not well highlighted in the literature. The follow-up of this patient indicated multiple lung metastatic deposits in a scan three months after IVC thrombectomy. Soon after the surgery he was placed on TKI. Pulmonary embolism is indeed a devastating complication caused by tumour thrombus shedding due the manipulation of the IVC during surgery; the mortality rate could be up to 75%.¹⁸⁾

For high-risk patients, the European Association for Urology (EAU) guidelines recommend the first CT six months after surgery and, subsequently, once a year up to three years and every two years afterwards. A recent report by Elahmadawy et al.,¹⁹⁾ about detection of local and distant disease relapse in surgically treated patients with

RCC, indicated that local and/or distant disease relapse was confirmed in 72% of patients. Regarding local recurrence, fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET-CT) showed specificity of 100%, compared to 98.6% with contrast-enhanced CT ($P > 0.05$) and higher sensitivity noted with contrast-enhanced CT (100%) compared to 96% with FDG PET-CT.

The limitations of this study are that it is retrospective and from a single institute. Despite these limitations, it appears to be safe to perform an IVC thrombectomy with a multidisciplinary approach in a developing world university.

Conclusion

The IVC thrombectomy, along with radical nephrectomy for renal cell carcinoma, can be performed with acceptable morbidity and mortality in level 1 to 3 tumour thrombus extension.

Disclosure Statement

The authors have no conflict of interest.

Author Contributions

Study conception: all authors

Data collection: ZUR

Writing: ZUR

Funding acquisition: nil

Critical review and revision: all authors

Final approval of the article: all authors

Accountability for all aspects of the work: all authors

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