

Renal Cell Carcinoma with Inferior Vena Cava Thrombectomy and Single-center Surgical Experience of 3 Years – A Case Series

ABSTRACT

Objective: The aim of the study was to report our experience of clinical outcomes and complications of open radical nephrectomy with inferior venacaval thrombectomy in patients with renal cell carcinoma as per new Clavien-Dindo method and compare with our previously published data. **Patients and Methods:** Total 13 patients who underwent radical nephrectomy and inferior vena cava (IVC) thrombectomy without the help of cardiopulmonary bypass between January 2017 and December 2019 were included in this retrospective analysis. Data were collected and analyzed by SPSS software and compared with our previous published data. **Results:** The median age was 55 years, and 10 (76%) of them were men. Surgery was done by midline abdominal incision. The median duration of surgery was 289 min and median blood loss was 1061 ml. The extent of tumor thrombus was intrahepatic in eight, retro hepatic in four, and suprahepatic in one patient. Complications as per Clavien Dindo Classification were anemia (Hb <8 mg/dl) requiring transfusion of blood products (Gr.II) in all patients. In immediate post-operative period, 1 (7%) patient developed acute kidney injury (Gr.I), 4 (30%) patients had evidence of hypotension (Gr.II), while 2 (15%) patients required hemodynamic support. Paralytic ileus (Gr.I) was seen in 1 (7%) patient and 2 (15%) patients had symptoms of cough and breathlessness due to atelectasis (Gr.I) of the lower lobes of lungs. Finally, one patient had sepsis (Gr.IVa), one patient had partial wound dehiscence (Gr.IIIa) requiring secondary suturing under local anesthesia and one patient eventually progressed to chronic kidney failure (Gr.IVa) requiring intermittent dialysis. At median 3-year follow-up, 12/13 patients are alive and well and one patient developed local relapse and is on targeted therapy. **Conclusion:** Radical nephrectomy with IVC thrombectomy still remains the most effective therapeutic option in the management for renal cell carcinoma with IVC thrombus. Although this is complicated surgery, our data suggest that with multi-disciplinary approach not only complications can be reduced but excellent survival outcome can be achieved. Finally, with the help of new Clavien an Dindo classification, there is a uniformity in classifying the complications which can be used to compare with other studies later on.

Key words: Clinical presentation, Complications and prognosis, Inferior vena cava thrombus, Renal cell carcinoma, Surgical management

INTRODUCTION

Tumor thrombus within the venous drainage system of the kidney can occur with many retroperitoneal tumors including renal cell carcinoma (RCC). Of them, 18% of all tumors that have venous thrombi are due to RCC.^[1] In adults, however, non-RCC tumors such as urothelial carcinoma of the renal pelvis, lymphoma, retroperitoneal sarcoma, adrenocortical carcinoma, pheochromocytoma, and angiomyolipoma are other potential sources of an inferior vena cava (IVC) thrombus.^[2,3] We have also reported an adrenal tumor having IVC thrombus.^[4] Management of such a clinical setting of RCC with IVC thrombus is technically challenging and necessitates multidisciplinary approach.

At our institution, radical nephrectomy with IVC thrombectomy program was started since 1994 and we have reported our experience in 2007^[5] and 2012.^[6] In 2017, we prospectively started using Clavien Dindo method^[7] of reporting the complications which forms the basis of this

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review. This review is mainly to report the outcomes and complication as per new Clavien and Dindo method.^[7]

MATERIALS AND METHODS

We performed a retrospective review of open radical nephrectomy with or without IVC thrombectomy database

between January 2017 and December 2019. We identified 13 patients who had undergone radical nephrectomy with IVC thrombectomy without circulatory bypass. Patients with thrombi involving only the renal vein were excluded from the study. We stratified patients by thrombus level at the time of surgery^[8] [Figure 1], also by surgical approach to the IVC (IVC controlled above versus below the liver). Tumors with infra-hepatic IVC involvement are approached by midline abdominal incision.^[5] After mobilization of small and large bowel, gentle complete dissection of kidney is done.

Proximal and distal control of IVC and opposite renal vein is obtained. Tourniquets snugged and IVC is opened and thrombus is milked out. IVC repair done after flushing out air followed by radical nephrectomy. Tumors with retro hepatic and suprahepatic below diaphragm were also approached by midline abdominal incision, after carrying out the same technique of bowel mobilization, liver dissection was done and suprahepatic control of IVC was taken and IVC was opened to remove the thrombus.^[9] Various intraoperative and post-operative complications were recorded, categorized, and graded using a modified version of the Clavien-Dindo system. Complication data were confirmed through careful review of all patient charts and outpatient notes. There was the lack of consensus on how to define and grade adverse post-operative events which has greatly hampered the evaluation of surgical procedures. A new Clavien Dindo classification of complications was initiated in 1992 and was updated in 2004. It is based on the type of therapy needed to correct the complication. The principle of the classification was to be simple, reproducible, flexible, and applicable in all fields of surgery; the main aim for developing this classification was to eliminate subjective, inaccurate, or confusing terms such as “minor or major” and provide a uniformity in defining the complications.

Complications were recorded up to 3 weeks after surgery. Thromboembolic events (deep vein thrombosis or pulmonary embolus) were radiographically confirmed. Ileus was defined as the inability to tolerate oral feeding by post-operative day 5 or nausea, vomiting or distension requiring nasogastric drainage, fluid support, or parenteral nutrition. Complication grades ≥ 3 are considered major complications. Patients were also grouped according to Charlson comorbidity index (CCI) as per their morbidities.

RESULTS

Between January 2017 and December 2019, 55 patients underwent resection of renal masses in our institute. IVC involvement was present in 13 (23%) of them. The median (interquartile range) age of the group was 55 (33–66) years.

Out of 13 patients, 10 (77%) of them were men and 3 (23%) were female [Figure 2]. Overall health status of a patient before surgery was assessed with the help of American Society of Anesthesiologists score (ASA). This allowed

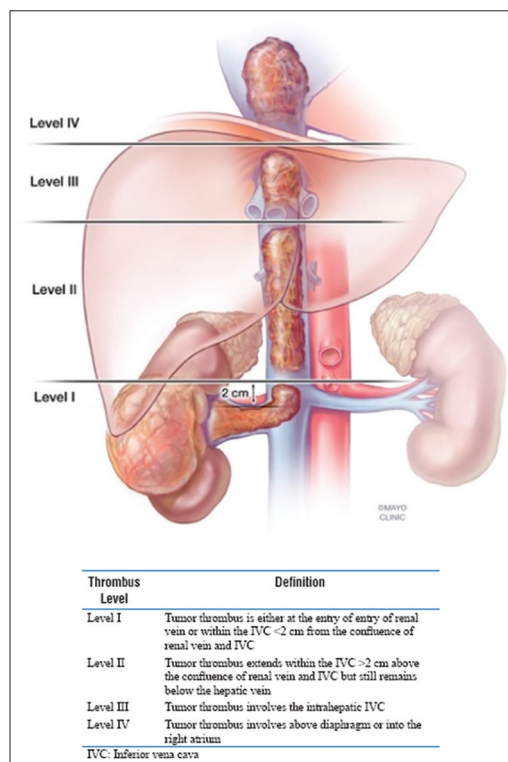


Figure 1: Level of thrombus

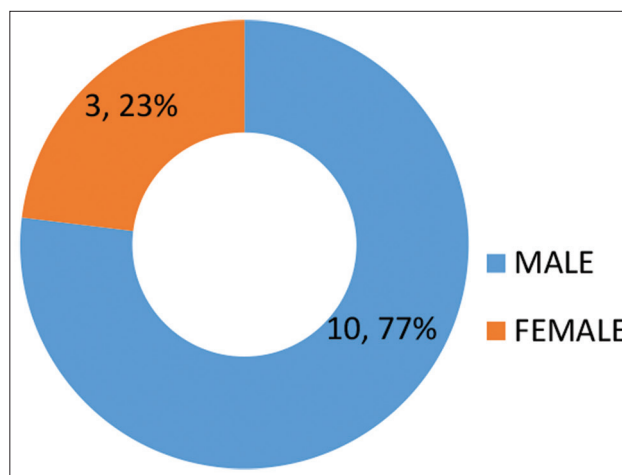


Figure 2: Sex distribution

patients outcome to be stratified by a general assessment of illness severity.

At presentation as per the Figure 3, 7 (53%) patients were categorized into Class 1, while 4 (30%) patients into Class 2 and 2 (23%) patients into class 3. Four (30%) presented to the outpatient clinic with incidentally detected renal mass with radiological investigation carried out for some other cause, while 7 (53%) had vague abdominal symptoms such as pain, LUTS, and hematuria while only 2 (23%) patients presented

with systemic symptoms of fever, pedal edema, dyspnea, and palpable flank mass.

The original CCI chart review instrument designed by Charlson, and colleagues produced a morbidity score that reflects mortality risk. The score is determined based on 19 medical conditions and adjusts for variable morbidity rates within a patient population.

As shown in Figure 4, as per CCI, 6 (46%) patients were had no comorbidities, while 5 (38%) were having CCI of 1 and only 2 (15%) patients had serious comorbidities with a CCI score of 2. Furthermore, fitness for surgery and post-operative morbidity was calculated in respect to the basal metabolic rate (BMR) of the patients, and 3 (23%) were normal with BMR of 18.5–25 kg/m², while 4 (30%) patients were overweight with BMR of 25–30 kg/m² and 6 (46%) were obese with BMR of >30 kg/m².

As per personal history, as shown in Figures 5 and 6, out of 13 patients (46%) were chronic smokers, three out of 13 patients (23%) were diabetic with HBA_{1c} of >6, and five out of 13 patients (38%) patients were hypertensive with two readings of blood pressure of more than 140/90 mmHG.

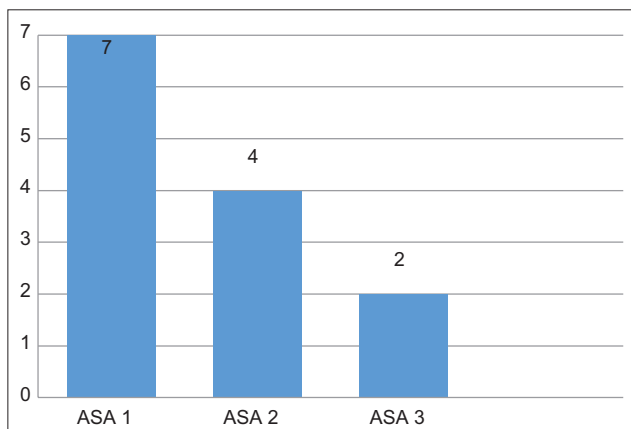


Figure 3: ASA score

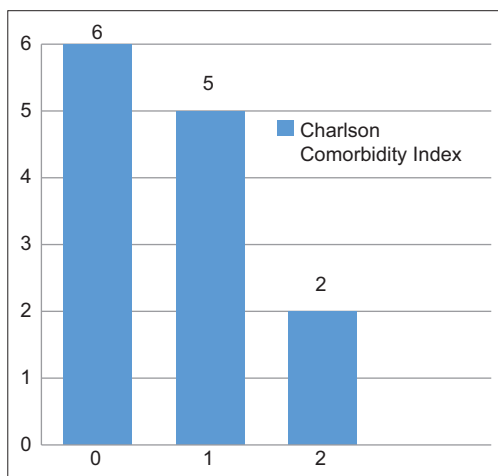


Figure 4: Charlson comorbidity index

Estimated glomerular filtration rate (GFR) was calculated with the help of chronic kidney disease-epidemiology collaboration (CKD-EPI) formula to assess pre-operative kidney function. 7 patients (53%) had normal GFR, while 3 patients (23%) had Grade 1, 2 patients (15%) had Grade 2, and 1 patient (7%) had Grade 3 of CKD.

The median duration of surgery was 289 (240–360) min, and median blood loss was 1061 (600–1500) ml.

As per the data of intraoperative and post-operative findings, blood transfusion was required for all 13 patients intraoperatively and postoperatively. There was no case of gastrointestinal tract, pulmonary, hepatic, or any other soft-tissue injury intraoperatively.

In immediate post-operative period, 1 (7%) patient developed acute kidney injury with raised serum creatinine of more than 2 times the pre-operative value. Four (30%) patients had hypotension and two patients required hemodynamic support for maintaining mean arterial pressure of >80 mmHg.

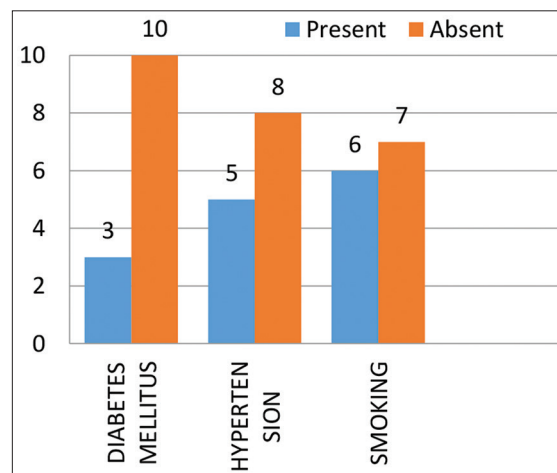


Figure 5: Personal history

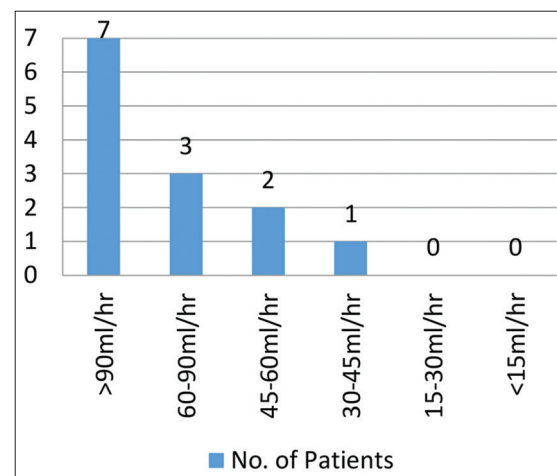


Figure 6: Renal function (eGFR)

One (7%) patient had paralytic ileus and was managed conservatively. In early postoperative period, after 72 h, 1 (7%) patient had acute renal failure with increase in creatinine to >3 times the pre-operative value and required dialysis once. Two (15%) patients had symptoms of cough and breathlessness due to atelectasis of the lower lobes of lungs, which was managed by aggressive physiotherapy and oxygen supplements. Two (15%) patients showed more than 150cc daily drain output for more than 72 h which later subsided conservatively while one patient experienced symptoms of deep vein thrombosis, which was managed by physician medically.

Only one patient developed symptoms of sepsis with high-grade fever, decreased urine output which was managed by aggressive antibiotic therapy and hemodynamic management. On follow-up, only one patient experienced wound infection and partial dehiscence which was managed by regular dressing and secondary suturing under local anesthesia and one patient eventually progressed to chronic kidney failure from preexisting marginal kidney functions.

DISCUSSION

RCC has a unique characteristic feature of vascular invasion.^[10] RCC extends into IVC forming a tumor thrombus. This tumor thrombus if untreated can even extend till right atrium.^[11] Surgical treatment in the form of radical nephrectomy with IVC thrombectomy still remains treatment of choice in such patients.^[12] The surgical procedure by itself is of such magnitude that it should be performed by best available expertise and in multidisciplinary center foreseeing the complexity of the procedure. The current review focuses on clinical presentation, intraoperative findings, tumor pathology, post-operative course, and oncological outcomes of patients undergone radical nephrectomy with IVC thrombectomy.

Patient selection criteria

Patient selection is a key factor in view of successful outcome. Older age and associated comorbidities do hamper the post-operative recovery.^[13] In our study, the youngest age of our patient was 33 years and oldest was 66 years with a median age of 55 years. Three out of 13 patients were diabetic and five out of 13 patients were hypertensive. Distant metastasis in another factor to be considered while selecting patients for operative intervention.^[14] In our study, none of the selected patients had evidence of distant metastasis.

Surgical expertise and hospital factor

Radical nephrectomy with IVC thrombectomy is a complex procedure to perform. It should always be performed by best expertise and in centre where all necessary facilities are available. Even though our all-surgical procedures performed where without the use of heart-lung machine, we advise and kept the equipment on stand-by mode if required in emergency.

Table 1: Complications

Intraoperative		No. of patients	
Blood transfusion		13	
Immediate post-operative		Clavien Dindo classification	No. of patients
Blood transfusion	Grade II		13
Acute kidney injury	Grade I		1
Hypotension	Grade II		4
Late post-operative			
Sepsis	Grade Iva		1
Wound infection	Grade II		1
Wound dehiscence	Grade IIIa		1
Chronic renal failure	Grade Iva		1
Early post-operative			
Ileus	Grade I		1
Anemia (Hb <8 g/dl)	Grade II		10
Acute renal failure	Grade IVa		1
Pulmonary atelectasis	Grade I		2
Ascites	Grade I		2
Deep vein thrombosis	Grade II		1

We recommend undertaking this procedure by experience surgeon and in centers where all the facilities are available.

Level of thrombus

Aggressive treatment should be done in patients with IVC thrombus.^[15] IVC involvement is more common on the right side due to short renal vein.^[16] Knowing the extent of IVC thrombus involvement preoperatively helps in staging and planning the surgery. Patients who undergo only nephrectomy in spite of having IVC thrombus ends up with very poor prognosis and high mortality rate.^[17] In our study, 8 patients (61%) had infrahepatic IVC thrombus, 4 patients (30%) had retrohepatic, and 1 patient (9%) had suprahepatic IVC thrombus. In today's era of advanced technology, even though options of angioscopically guided endoluminal intervention are present but availability and feasibility of such technique is still evolving. Hence, we believe that our experience open IVC thrombectomy still provides a good result and has good prognosis.

Staging

Many different types of staging system are available for macroscopic vascular involvement in RCC. We have used Mayo's classification in our series.

Primary TNM classification is also used for classification of primary malignancy. IVC involvement below diaphragm (T3b), above diaphragm (T3c), or invasion into wall of vena cava at any level as T3c is considered as an important adverse factor.^[20] MRI is considered as the most accurate investigation to classify IVC thrombus and also to detect involvement if

TABLE 2: COMPLICATIONS

COMPLICATIONS	MATTHEW ET AL. 2010	KULKARNI ET AL. 2007	KULKARNI ET AL. 2012	PRESENT STUDY
BLOOD TRANSFUSION	65%	-	-	100%
SEPSIS	1%	6%	13%	7%
ACUTE RENAL FAILURE	9%	15%	17%	7%
CEREBROVASCULAR EVENTS	4%	5%	3%	0%
PARALYTIC ILEUS	10%	12%	10%	7%
PULMONARY ATELECTASIS	11%	-	-	15%
WOUND DEHISCENCE	-	1.5%	1%	7%
MORTALITY	6%	3.5%	2%	0%

IVC wall by tumor as it is important for staging and planning the operative procedure.^[18]

Surgical technique

Tumors with infrahepatic IVC involvement are approached by midline abdominal incision. After mobilization of bowel and caudate lobe of liver, gentle complete dissection of kidney is done. Proximal and distal control of IVC and opposite renal vein is obtained. Tourniquets snugged and IVC is opened and thrombus is milked out. IVC repair done after flushing out air followed by radical nephrectomy. Some authors advocate alternative technique for suprahepatic IVC involvement such as temporary occlusion of intrapericardial IVC or veno-venous bypass or application of supradiaphragmatic aortic cross clamp.^[19,20] However, they have serious side effects as hypotension, increased bleeding from hepatic veins or paraplegia, and intestinal gangrene, respectively. We concur with the benefits of team approach of urologist, cardiac surgeon, cardiac anesthetist, and cardiac theater facilities.

Complications

Radical nephrectomy with IVC thrombectomy is a complex procedure.^[21] We classified the complications of our study into intraoperative, immediate post-operative, early and late post-operative as mentioned in Table 2.

When data of our first study in 2010 were compared to the present study we noted, incidence of sepsis was 6% while in our study, it was 7%, transient renal failure was 15%, while we had 7%, cerebrovascular event (CVE) episodes 4% versus 0%, subacute intestinal obstruction 12% versus 7%, burst abdomen of 1.5% versus 7%, and total mortality of 3% versus none in the present series. Similarly, in our second study, data 2012 were compared to our present study, we found transient renal dysfunction 17% versus 7%, malaria 3% versus none, intestinal obstruction 10% versus 7%, CVE 3% versus none and total mortality of 2% versus none. Last, we compared in Kaag *et al.*,^[22] 2010, CVE 4% versus none, gastrointestinal 10% versus 7%, renal 9% versus 7%, thromboembolic 5%

versus 0%, pulmonary 11% versus 15%, and wound infection and dehiscence 1% versus 7%.

The original CCI was designed by Charlson, and colleagues produced a morbidity score that reflects mortality risk. The score is determined based on 19 medical conditions and adjusts for variable morbidity rates within a patient population.^[23] In our study, we classified patient according to CCI and had no mortality across any categories of CCI.

Thus, we feel that the uniformity in defining the complications using the new Clavien Dindo classification has helped us define and identify the major complications in early period of occurrence. Appropriate preventive measures and treatment of such complications in early period has helped us to reduce the morbidity and mortality in our study.

CONCLUSION

Our study emphasizes that radical nephrectomy with IVC thrombectomy still remains the most effective therapeutic option in the management for renal cell carcinoma with IVC thrombus. Although this is a complicated surgery, good success rate can be achieved with multi-disciplinary approach leading to excellent survival outcome with reduced morbidity and mortality. Further with the help of new Clavien Dindo classification, there is a uniformity in classifying the complications which can be used to compare with other studies.

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