Resection of Renal Tumors Invading the Vena Cava

Chad Wotkowicz, MD*, Matthew F. Wszolek, MD, John A. Libertino, MD

KEYWORDS

- Renal cell carcinoma Inferior vena cava
- Surgical management

Renal cell carcinoma (RCC) has been called the "internists' tumor" for many years because of the myriad of vague symptoms associated with this malignancy. Patients historically presented with metastatic disease at the time of their initial diagnosis. At the present time, approximately 70% of the patients who have RCC are diagnosed as a result of enhanced imaging capabilities. This early diagnosis has produced a stage migration because many RCCs are discovered incidentally. Kidney cancer is the third most common urologic malignancy in the United States, representing 3.5% of the newly diagnosed cancers in the United States, and accounts for 2.3% of cancer-related deaths.¹ During the past 20 years, the incidence of RCC has been increasing worldwide at a rate of 2.5% every year. This increased incidence is a result of increased abdominal imaging and an aging population.^{2–4} In addition, RCC is a highly vascular malignancy with a tendency to invade the venous system and create a tumor thrombus either in the renal vein or the inferior vena cava (IVC). An estimated 4% to 10% of RCCs have a tumor thrombus present in the venous circulation, specifically the renal vein and IVC, and a subpopulation of 1% has extension into the right atrium.⁵ Despite advances in radiation, chemotherapy, and immunotherapy the reference standard for RCC with tumor thrombus remains surgical resection. Several contemporary series have demonstrated 5-year survival rates of up to 60% in the absence of metastatic disease in patients who have venous tumor thrombus treated with radical nephrectomy and tumor thrombectomy.5-11

CLINICAL PRESENTATION

The advent of cross-sectional imaging for the work-up of abdominal pain has resulted in an increase of RCC prevalence. A number of patients who have venous tumor thrombus can be asymptomatic depending on the level of the tumor thrombus and the extent of occlusion of the IVC. Significant venous congestion as a result of caval intrusion can present with varying symptoms, including significant lower extremity edema, varicocele formation, proteinuria, caput medusae, and even pulmonary emboli. If the tumor extends above the level of the hepatic veins, Budd-Chiari syndrome may result from obstruction of the major hepatic veins, resulting in a triad of hepatomegaly, abdominal fullness/pain, and ascites. The resulting varices produce massive collaterals with associated impaired hepatic function and portal hypertension. Additional symptoms of RCC include flank discomfort, hematuria, and constitutional changes (fever, weight loss, fatigue). These constitutional symptoms usually indicate the presence of metastatic disease with an overall poor prognosis.

DIAGNOSTIC IMAGING AND PREOPERATIVE EVALUATION

All patients who have renal masses must have imaging studies, including chest radiographs and bone scans when appropriate, to rule out metastatic disease. In patients who have venous extension, additional studies are necessary to define the extent of the tumor thrombus. For this subset of

Department of Urology, Lahey Clinic, Burlington, MA, USA * Corresponding author. *E-mail address:* Chad.wotkowicz@lahey.org (C. Wotkowicz).

Urol Clin N Am 35 (2008) 657–671 doi:10.1016/j.ucl.2008.07.013 0094-0143/08/\$ – see front matter © 2008 Elsevier Inc. All rights reserved.

Wotkowicz et al

patients the authors' preferred imaging modality is MRI, specifically magnetic resonance venography, in combination with CT studies and threedimensional reformatted images (**Fig. 1**). Tumor at or above the level of the diaphragm requires transesophageal echocardiography and may necessitate angiography to delineate the extent of the tumor thrombus. At the present time positron emission tomography (PET) scans have a limited diagnostic role; however, this modality is being evaluated at the Lahey Clinic as part of the preoperative evaluation and postoperative follow-up. The authors have noted that PET CT has demonstrated lesions in the liver that have not been detected on ordinary CT or MRI (**Fig. 2**).

A report from Zini and colleagues¹² suggests that preoperative measurements of the renal vein and IVC diameter with associated tumor thrombus correlate with the rate of renal ostial wall invasion and may serve as another prognostic indicator.

The importance of preoperative imaging for surgical planning cannot be overemphasized. Tumor thrombus extending to the level of the hepatic veins or higher may require cardiopulmonary bypass and circulatory arrest to provide insurance against excessive blood loss. Patients slated for cardiopulmonary bypass and circulatory arrest should have a cardiac evaluation, which may include stress testing or a coronary angiogram. If significant coronary artery disease is discovered, it may be treated with either a stent or bypass grafting. In five of the authors' patients bypass grafting was performed concomitantly with the radical nephrectomy and IVC thrombectomy.¹³ Bland thrombus often can be distinguished from tumor thrombus during the preoperative evaluation, and anticoagulation therapy or placement of an IVC filter should be considered to limit further propagation and the possibility of a pulmonary embolus. Transesophageal echocardiography identifies the presence of tumor thrombus in the right atrium and is an important adjunctive intraoperative diagnostic modality.¹⁴

RENAL ANGIOINFARCTION

Although only one prospective trial of preoperative angioinfarction is available to validate its use, the authors find that preoperative renal artery embolization is an important adjunctive tool in the treatment for advanced RCC, including patients who have venous tumor involvement.¹⁵ Preoperative renal angioinfarction facilitates the dissection of the renal tumor as a result of local tissue edema from hypoxia and tissue necrosis. In addition, it potentially may decrease the extent of the tumor thrombus while minimizing intraoperative blood loss associated with extensive venous collaterals. Renal angioinfarction also allows the surgeon to ligate or transect the renal vein before controlling or occluding the renal artery. Clinicians must be aware of the postinfarction syndrome caused by innate and humoral immune responses to the infracted kidney.¹⁶ This syndrome is characterized by chills, fevers, flank pain, malaise, hematuria, transient hypertension, and hyponatremia, all of which are self limiting.¹⁷



Fig. 1. (*A*) Coronal scan demonstrates the extent of tumor thrombus to the level of the major hepatic veins. (*B*) Lateral reconstructions indicate thrombus above the diaphragm. Cardiopulmonary bypass was required to resect this tumor.



Fig. 2. PET scan obtained during preoperative evaluation for planned radical nephrectomy demonstrates increased uptake in multiple sites of the liver.

CLINICAL STAGING AND PROGNOSTICS FACTORS

There have been numerous proposals for staging RCCs and venous invasion. The current TNM staging system (Box 1) designates tumor thrombus in the renal vein up to the diaphragm as T3b. Numerous retrospective studies at the Lahey Clinic and elsewhere advocate revision based on difference in survival when only the renal vein is involved.^{18,19} Literature, however, supports the current classification scheme, leaving the debate open for further discussion.²⁰ In addition to the level of the tumor thrombus, a variety of centers are exploring additional prognostic factors for a revision of the current staging. The UCLA Integrated Staging System incorporates TNM stage, Fuhrman tumor grade, and the Eastern Cooperative Oncology Group performance status.²¹ Kattan and colleagues²² have developed a nomogram based on the TNM stage, patient symptoms, tumor size, grade, and vascular invasion or tumor necrosis. The SSIGN (stage, size, grade necrosis) model from the Mayo Clinic also has been evaluated in more than 1800 patients.²³

SURGICAL TREATMENT STRATEGIES

This discussion of surgical planning covers the following levels of tumor thrombus: renal vein, infrahepatic, retrohepatic, suprahepatic, supradiaphragmatic, and intra-atrial. Aggressive surgical management (radical nephrectomy, IVC

Box 1

American Joint Committee on Cancer 2002 TNM staging system for renal cell carcinoma

T: Primary tumor

Tx: Primary tumor cannot be assessed

T0: No evidence of primary tumor

T1: Tumor <7 cm in diameter, limited to kidney

T1a: Tumor 0–4 cm in greatest diameter, confined to kidney

T1b: Tumor 4–7 cm in greatest diameter, confined to kidney

T2: Tumor > 7 cm in greatest diameter, confined to kidney

T3: Tumor extends into major veins or invades adrenal gland or perinephric tissues but not beyond Gerota's fascia

T3a: Tumor directly invades adrenal gland or perirenal and/or renal sinus fat but not beyond Gerota's fascia

T3b: Tumor grossly extends into the renal vein or its segmental (ie, muscle-containing) branches or into the vena cava below the diaphragm

T3c: Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava

T4: Tumor invades beyond Gerota's fascia

N: Regional lymph nodes

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Metastasis in a single regional lymph node N2: Metastasis in more than one regional lymph node

M: Distant metastases

MX: Metastases cannot be assessed

M0: No distant metastases

M1: Distant metastases

thrombectomy, lymph node dissection, and potential metastectomy) remains the primary treatment modality, with the level of the tumor thrombus dictating the surgical approach. Tumors involving the caval venous system represent one of the most technically challenging and rewarding procedures for urologists because the 5-year survival rates, even in the face of intra-atrial tumor thrombus, are comparable to those for lesions confined to the kidney. A stepwise approach is discussed for each level of vein involvement focusing on techniques the authors have found successful in treating more 243 patients over a 30-year period (**Fig. 3**).²⁴ Additional techniques used by other urologic surgeons also are discussed in conjunction with specific scenarios.

RENAL VEIN INVOLVEMENT

The invasion of the tumor thrombus at the level of the renal vein often can be approached using the principles of traditional radical nephrectomy first described by Robson and colleagues²⁵ in 1969. The kidney and the great vessels can be exposed, mobilized, and controlled using a thoracoabdominal incision (Fig. 4). In general a ninth or tenth intercostal incision is preferred. Significant venous collaterals can develop in the setting of venous tumor thrombus, particularly the lumbar drainage system. After ligation of the renal artery, the tumor thrombus is palpated gently to ensure that no further extension into the vena cava is present. A Satinsky clamp then is placed at the level of the renal vein ostium, sparing any lumbar tributaries. A circumferential incision is made at the level of the renal vein ostium. The caval defect is closed with running 4-0 polypropylene sutures, with caution taken to avoid constricting the diameter of the vena cava. With the venous system and arterial system ligated, a standard nephrectomy is performed with or without a lymph node dissection for staging purposes. In rare instances it is possible to spare the adrenal gland in lower pole tumors.

SUPRARENAL (INFRAHEPATIC TUMOR THROMBUS)

The authors categorize the presence of tumor thrombus below the level of the liver edge as infrahepatic. It often is possible to resect these lesions without bypass, because caval wall resection is rarely necessary, and bleeding can be controlled. The initial portion of this operation is to control



Fig. 3. Surgical stratification of renal cell cancer with tumor thrombus at the Lahey Clinic.



Fig. 4. Thoracoabdominal incision landmarks.

the IVC with limited manipulation to prevent tumor embolus. The vena cava is dissected anteriorly and mobilized so that a Rummel tourniquet can be placed above and below the tumor thrombus and around each renal vein. Transesophageal echocardiography is performed to rule out propagation of the tumor thrombus. A chevron incision is made from the tip of the eleventh rib to the tip of the contralateral eleventh rib. The aorta and vena cava are exposed, and dissection is continued to allow placement of the Rummel tourniquets. As mentioned previously, large upper pole tumors also can be approached via a thoracoabdominal incision. The renal artery, associated lumbar and minor hepatic veins, and the contralateral renal vein are isolated and are dissected circumferentially. In many instances renal angioinfarction may produce an inflammatory response that precludes arterial mobilization; in this instance the authors defer ligation of the renal artery until the tumor thrombectomy has been completed. After the Rummel tourniquets are applied as described previously, a longitudinal cavatomy is made, and the thrombus is freed from the caval wall to the level of the renal vein ostium (Fig. 5) The IVC then is gently flushed with heparinized saline and is evaluated for residual fragments. The cavotomy is closed with continuous 4-0 polypropylene sutures. The infrarenal clamp is released initially to purge the system and to limit the chance of embolus. Radical nephrectomy and/or lymph node dissection is performed after closure of the vena cava has been completed.



Fig. 5. Removal of larger rightsided infrahepatic tumor without cardiopulmonary bypass.

SUPRARENAL THROMBUS (RETROHEPATIC AND SUPRADIAPHRAGMATIC)

Surgical removal of RCC with suprarenal retrohepatic tumor thrombus can be accomplished with a variety of surgical techniques with equivalent oncologic outcomes. The authors' experience with hypothermic circulatory arrest and cardiopulmonary bypass is one of the largest series published to date with outcomes comparable to those of contemporary colleagues.²⁶ The authors have described techniques of vascular and liver mobilization that have provided excellent exposure to the retrohepatic portion of the IVC (**Fig. 6**). After a chevron incision is made and the absence of metastatic disease is confirmed, the anterior surface of the IVC is identified and is palpated gently to confirm the cephalad extent of the tumor thrombus. In some cases the thrombus can be gently milked caudally for clamp placement. This procedure must be performed with caution to prevent embolization of the thrombus. Traditionally the duodenum is kocherized, and the Langenbuch maneuver is used to mobilize the liver cephalad and to the left, thus exposing the retrohepatic portion of the IVC (Fig. 7). The kidney is mobilized completely with the exception of the renal vein and associated tumor thrombus (Fig. 8). The IVC then is mobilized completely from the renal vein to the cephalad extent of the tumor thrombus, ensuring retroperitoneal hemostasis before heparinization and cardiopulmonary bypass. The right subclavian artery and superior vena cava are cannulated, and cardiopulmonary bypass is initiated (Fig. 9). Thiopental and methylprednisolone are given as the core temperature is cooled to 18° to



Fig. 6. (A, B) Anatomic relationship of IVC, hepatic vasculature, and diaphragm.



Fig. 7. Exposure of the retrohepatic IVC.

20°C and the patient is exsanguinated. Patients can withstand up to 40 minutes of circulatory arrest time without neurologic insult and may be exposed to extended periods with the use of retrograde cerebral perfusion.²⁷ A right atriotomy provides distal control of the tumor thrombus, minimizing the risk of embolization (Fig. 10). An anterior cavotomy is made from the level of the renal vein to the level of the hepatic veins, and the thrombus is extracted with the patient in Trendelenberg's position and using positive-pressure respiration (Fig. 11). In some situations a Fogarty catheter is passed into the atrium and/or hepatic veins to retrieve portions of the tumor thrombus. The authors use venacavascopy with a flexible cystoscope to ensure that tumor thrombus removal is complete. Efforts should be made to



Fig. 8. Intraoperative photograph demonstrating the complete mobilization of the kidney except for the renal vein and associated tumor thrombus.

remove the kidney and thrombus as one specimen (**Fig. 12**). The advantage of bypass is an essentially bloodless operative field, but the authors recognize and accept the complications of bypass, including coagulopathy and the potential for neurologic complications.

MINIMALLY INVASIVE CARDIOPULMONARY BYPASS

Cardiopulmonary bypass has been done at the Lahey Clinic using a minimally invasive approach since 1998.²⁸ It was developed initially for aortic valve replacements but suited the authors' need to carry out cardiopulmonary bypass and circulatory arrest in patients who have tumor thrombus extending beyond the hepatic veins or into the atrium.²⁹ Unlike the traditional approach, the kidney is not mobilized during the initial exposure; rather, a chevron incision is made, and surveillance for intra-abdominal metastatic disease is performed. The anterior vena cava and renal vein are identified using a "no-touch" technique, minimizing the possibility of a pulmonary embolus. (The initiative for this approach stemmed from a lethal pulmonary embolism during the removal of a large left-sided adrenal tumor with associated retrohepatic tumor thrombus.)

Next, the right subclavian artery is mobilized via a small infraclavicular incision. Then a small (2-inch) right parasternal incision is made at the heads of the third and fourth ribs. This incision allows resection of the rib cartilage and ligation of the right internal thoracic artery. Periosteum muscles and pleura are preserved for closure, and the right pericardium is opened exposing the superior vena cava and right atrium. Systemic heparinization is initiated as an 8-mm synthetic graft is sewn to the right subclavian artery for arterial return while a twostage venous cannula is positioned into the right atrium for venous outflow (Fig. 13). Cardiopulmonary bypass then is initiated, and the patient is cooled in a fashion similar to that used for patients undergoing traditional bypass procedures. A formal right atriotomy is made, and the distal components of the thrombus are identified while the urologic surgeon opens the IVC. Tumor thrombus is removed from the cava, and a sponge stick or laparotomy pad is passed up to the cardiothoracic team to be certain that all residual thrombus has been removed (Fig. 14). Flexible cystoscopy may be performed to confirm the presence or absence of clot or venous wall invasion. Fogarty balloons may be used to address thrombus in the hepatic veins. Radical nephrectomy is performed while the



Fig. 9. Traditional cardiopulmonary bypass requiring median sternotomy.

patient is being rewarmed and is coming off bypass. Then protamine sulfate is given to offset the effect of heparin; fresh frozen plasma, platelets, and desmopressin can be to given to address any coagulopathy. Unlike traditional bypass, coronary revascularization cannot be done.

The authors have performed more than 50 caval thrombectomies using cardiopulmonary bypass and circulatory arrest. They have performed minimal-access bypass procedures in more than 30 patients to date with results demonstrating shorter operative and hospital times and decreased rates of transfusion and of mechanical ventilatory support (Table 1).²⁶ Eliminating the median sternotomy reduces the dose of postoperative analgesics required and also avoids reoperative sternotomy in patients who have had a prior coronary artery bypass procedure. Close monitoring for hematologic and neurologic complications must be observed in the immediate postoperative period.³⁰ Thus far these authors have had no serious neurologic sequelae from cardiopulmonary bypass and circulatory arrest in their experience of more than 50 patients.

VENOVENOUS BYPASS

Patients who have minimal extension of thrombus above the level of the diaphragm can be managed with venovenous bypass via a caval-atrial shunt.^{31,32} With this approach the vena cava needs to be controlled at the infrarenal level, at the level of both renal veins, and at its intrapericardial portion. Once control is established, the cannulas can be placed in the right atrium or axillary vein and the femoral veins, and bypass can be initiated before cavotomy. Bleeding from the hepatic venous system can be managed by cross-clamping the hepatic veins or by the Pringle maneuver. The Pringle maneuver can be used for up to 45 minutes before liver metabolism is affected significantly. Although this technique avoids cardiopulmonary bypass and circulatory arrest, the incidence of hepatic venous bleeding can be significant.



Fig. 10. Right atriotomy exposing tumor thrombus after circulatory arrest has been achieved.

LIVER TRANSPLANTATION MOBILIZATION

Mobilization of the liver has been used successfully to treat similar tumors except in cases with significant intra-atrial tumor thrombus burden. Liver mobilization avoids the use of bypass, as described by the authors' group and by Ciancio and colleagues.^{33–35} The liver is mobilized to the left after the division of the ligamentum teres, falciform ligament, triangular ligament, and superior coronary ligament of the liver. The porta hepatis is accessed via the foramen of Winslow, and the Pringle maneuver is employed. This technique provides excellent access to the retrohepatic portion of the vena cava and allows mobilization of the liver from the vena cava, leaving only the major hepatic veins in continuity. After liver mobilization the surgeon can palpate and milk the tumor thrombus caudally below the confluence of the hepatics veins to limit hepatic venous congestion associated with hepatic clamping. All cases are performed with the use of transesophageal echo monitoring.

SUPRADIAPHRAGMATIC AND ATRIAL TUMOR RESECTION WITHOUT BYPASS

A case report from D'Ancona and colleagues³⁶ describes the removal of a suprarenal tumor thrombus using extracorporeal circulation and deep hypothermic arrest without violation of the thoracic cavity. After exposure of the vena cava, the liver is retracted inferiorly to expose the pericardium at the level of the diaphragmatic insertion. Retraction again is facilitated via division of multiple perihepatic ligamentous structures, as described previously. A pericardial window permits cardiac defibrillation. Extracorporeal



Fig. 11. (*A*, *B*) Schematic demonstrating the removal of atrial tumor thrombus. When tumor burden is too large, the atrial component may be fractured and removed first.



Fig. 12. Radical nephrectomy specimen and associated tumor thrombus.

circulation is established via the right femoral artery and the right femoral and subclavian veins, and core hypothermia to 20°C achieved before circulatory arrest commences. Infrahepatic and suprahepatic longitudinal incisions provide access for thrombus removal. In contrast to other reports, a nephrectomy is performed while gaining access to the femoral circulation and before extracorporeal circulation is established. Chowdhury and colleagues³⁷ discuss another alternative for intra-atrial tumor thrombus using cardiopulmonary bypass, mild hypothermia, and an intermittent cross-clamping of the supraceliac aorta to avoid the risks associated with circulatory arrest.

ENDOLUMINAL OCCLUSION AND CAVAL THROMBUS

The authors have used Fogarty balloon catheters in efforts to eliminate thrombus from the vena cava or, in some instances, thrombus that has extended into the hepatic veins, into the contralateral renal veins, or caudally toward the common iliac bifurcation. Zini and colleagues³⁸ describe an alternative technique of transesophageal echocardiography-guided endoluminal occlusion cranial to tumor thrombus, eliminating the need for extensive caval mobilization. Although the inherent risk of emboli during catheter placement seems high, their series of 13 procedures (6 retrohepatic and 7 suprahepatic) included only one event, which was asymptomatic. The authors claim that extensive caval mobilization used with liver transplant techniques carries an even higher risk of emboli. This technique should be approached with caution when the thrombus seems to invade caval wall, as evidenced by resistance to the catheter placement.

LAPAROSCOPIC MANAGEMENT IN RENAL CELL TUMOR THROMBUS

Laparoscopy has been used in the successful resection of renal carcinomas with renal vein thrombus via pure and hand-assisted approaches. Intraoperative ultrasound can help establish the extent of thrombus and guide the placement of distal clamps.³⁹ Hand-assisted approaches using a subcostal incision also have been reported for



Fig. 13. Minimal access cardiopulmonary bypass using a parasternal incision.



Fig.14. Yankeur suction passed from the thoracic team into the infradiaphragmatic IVC.

treating tumors extending into the IVC.⁴⁰ Urologists at the Cleveland Clinic successfully removed a right atrial tumor thrombus in a calf model using combined laparoscopy and thoracoscopy with deep hypothermic circulatory arrest.⁴¹ Such approaches are sure to surface with the continuing rapid advances in minimally invasive surgical techniques.

NEPHRON-SPARING SURGERY AND TUMOR THROMBUS

The unfortunate patient who has a solitary kidney and RCC with associated tumor thrombus and decent performance status may be a candidate for nephron-sparing surgery. Sengupta and colleagues^{42–44} have reported their experience as well as additional case reports. These studies showed limited oncologic success and a relatively high rate of eventual completion radical nephrectomy. The authors recommend that urologists attempting these procedures be skilled in extracorporeal bench surgery, renal autotransplantation, and vena caval reconstruction with the caveat that achieving negative margins is more important than avoiding the need for renal replacement therapy.

INTERRUPTION OF THE INFERIOR VENA CAVA

Using MRI with gadolinium, Blute and colleagues⁴⁵ have devised an approach for treating

bland tumor thrombus in the setting of RCC to prevent unwanted pulmonary embolism. The authors reviewed 160 patients who had thrombus extending 2 cm and more above the renal vein and identified 40 patients who had total or partial venous occlusion and the presence or absence of associated bland thrombus. (It should be noted that any attempt to resect or ligate the IVC should be preceded by efforts to preserve the integrity of the lumbar drainage system.) Blute and colleagues recommend ligating no more than two lumbar veins. Patients who have a patent cava and no associated distal or bland tumor thrombus can be managed with cavatomy closure only. A partially occluded vena cava with distal pelvic bland thrombus can be managed with an interruption caval filter. Patients who have a totally occluded vena cava with associated bland thrombus are treated by IVC staple ligation. In the latter group, distal margins should be sent to pathology for frozen-section analysis. The outcomes for these groups fail to demonstrate any significant morbidity and thus support the use of these techniques in the management of retrograde bland tumor thrombus in this complex surgical population.

CAVAL RESECTION AND REPAIR

Tumor thrombus may invade the wall of the IVC directly in up to 23% of patients, usually at the ostium of the renal vein.46 At the Lahey Clinic, the authors have had success using polytetrafluoroethylene substitution grafts. In cases requiring median sternotomy and entry into the heart, the authors also have used a portion of pericardium to repair defects in the vena cava. An additional option includes autologous saphenous vein grafts. Perhaps larger tumor thrombus burden, as suggested by Zini and colleagues, should be treated with cavectomy and interposition grafts where appropriate. Previous publications, however, suggest that these grafts are associated with increased morbidity and mortality, and their use is not recommended at this time.

COMPLICATIONS

The incidence of complications often depends on the level of tumor thrombus and the surgical approach taken. Boorjian and colleagues⁴⁷ reviewed their experience with more than 650 patients undergoing nephrectomy and tumor thrombectomy and noted that the incidence of early (<30 days) and late complications correlated with thrombus level. Operative time and blood loss followed the same trend. The present authors have reported their experience with minimal-access

bypass ²⁰			
	TMS Median (n = 22)	MA Median (n = 28)	P-value
Operation	600 (295–995)	450 (270–761)	<.001
Cardiopulmonary bypass time	135 (50–217)	148 (86–265)	.527
Circulatory arrest	33 (12–90)	34 (17–62)	.880
Days ventilated	7 (1–110)	4 (1–46)	.032
Length of stay	26 (2–114)	12 (5–45)	.007
Transfusions	11 (4–50)	5 (2–15)	.002
Overall complications	17	21	1.000
Pulmonary	12	7	.264
Cardiac	12	13	.741
Renal	6	4	.311
Infection	10	7	.210
Hepatic	7	5	.331

Table 1 Operative and perioperative comparison of traditional (TMS) versus minimal-access (MA) cardiopulmonary bypass²⁶

Data from Wotkowicz C, Libertino J, Sorcini A, et al. Management of renal cell carcinoma with vena cava and atrial thrombus: minimal access vs median sternotomy with circulatory arrest. BJU Int 2006;98(2):289–97.

versus traditional approaches for circulatory arrest with deep hypothermic circulatory arrest, showing the former to have shorter operative time and length of stay, less need for mechanical ventilatory support, and fewer transfusions **Table 1**.²⁶

CYTOREDUCTIVE NEPHRECTOMY AND METASTECTOMY

Patients who have metastatic RCC face a poor prognosis, with a median survival of 8 months and a 2-year survival rate of 10% to 20%. A combined analysis of the two sentinel trials elucidating the benefits of cytoreductive nephrectomy (Southwest Oncology Group-8949 and European Organization for Research and Treatment of Cancer) revealed a survival benefit of 13.6 months for nephrectomy combined with interferon-alpha therapy versus 7.8 months for interferon therapy alone.⁴⁸ Retrospective data from the UCLA group suggest a more substantial survival benefit when interferon alpha is replaced with interleukin-2.49 The underlying mechanisms of improved survival with cytoreductive nephrectomy before systemic therapy are not fully understood. The reduction in growth factors, angiogenesis promoters, and inhibitory immunomodulators by primary tumor resection may enhance the efficacy of systemic immunotherapy compared with immunotherapy without prior cytoreductive nephrectomy.

First described by Barney and Churchill⁵⁰ in 1939, the resection of pulmonary metastasis remains an effective treatment for select patients.

Studies have attempted to define patient populations that would benefit from metastectomy through subgroup analysis. Favorable prognostic factors in resecting isolated pulmonary metastasis include preoperative performance status, completeness of resection, number of lesions (fewer than six), extent of lymph node involvement, and length of disease-free interval. Patients having synchronous lesions have significantly worse outcomes.^{51,52} Properly selected patients may have 5-year survival rates exceeding 50%.⁵¹ At the present time, metastectomy in nonpulmonary sites such as the liver and brain is controversial and should be considered investigational.

CLINICAL OUTCOMES

There has been a modest increase in the number of IVC thrombectomies performed by urological oncologists and in improved survival outcomes. These results can be attributed to improved imaging modalities and surgical planning as well as to technological advances in intraoperative anesthesia and postoperative intensive care management. **Table 2** summarizes recent reports from tertiary centers with significant experience in surgical management of RCC with tumor thrombus. The debate concerning the prognostic significance of tumor thrombus level with regards to the current TNM staging system may be resolved best by a multi-institutional meta-analysis.^{53–58}

Table 2	
Surgical outcomes for patients who had renal cell carcinoma and tumor throm	bus

Author, Year	No. Patients	TumorThrombus Stratification	Complications (%)	Operative Mortality (%)	Survival Outcomes: Cancer-Specific Survival (CSS) and Disease-Specific Survival (DSS) (%)
Blute 2007	659	0: renal vein (426) I: ≤ 2 cm above renal vein (73) II: at or above hepatic veins (93) III: above hepatic vein (35) IV: above diaphragm (32)	Early surgical complications Level 0: 12.4 Level 1: 17.8 Level II: 20.4 Level III: 25.7 Level IV: 46.9 Late complications Level 0: 24.4 Level 1: 28.8 Level II: 33.3 Level III: 34.3 Level IV: 37.5 Complications 1970–1989: 13.4 1990–2006: 8.1	1970–1989: 3.8 1990–2006: 2.0	5-year CSS Level 0: 49.1 Level 1: 31.7 Level 11: 26.3 Level 111: 39.4 Level 1V: 7 Level 0 versus I ($P = .002$) Level 1–IV ($P = .868$) pN0/pNx, pM0: 59 pN1/pN2,pM1: 6 Histologic features With tumor necrosis: 26 Without tumor necrosis: 61 With sarcomatoid: 3 Without sarcomatoid: 47 Perinephric fat invasion Present: 32 Absent: 56
Fijusawa 2007	55	Level 1–IV I: infrahepatic (22) II: intrahepatic (20) III: suprahepatic (10) IV: into atrium (3)	_	3.6	CSS (all levels) 1 year: 74.5 3 years: 51.4 5 years: 30.3
Kalatte and Belldegrun 2007	321	Renal vein: 166 IVC: 137 Atrium: 18	All complications Renal vein; 12 IVC: 28 Atrium: 11	Renal vein: 2 IVC: 7 Atrium: 11	DSS (2/5/10-year) Renal vein (58/41/24) IVC (48/30/25) Atrium (45/22/0) Thrombus level (P = .53) Overall immunotherapy response rate: 19 Metastatic disease Median survival: 16 months

Parekh and Smoth 2005	49	Nevus classification Level I: renal vein Level II: infrahepatic IVC Level III: retrohepatic to diaphragm Level IV: supradiaphragmatic	Major complications: 6 Minor complications: 16	8	Overall 3-year survival Negative lymph node: 75 Positive lymph node: 0
Ficarra and Patard 2001	142	Renal vein: 118 Subdiaphragmatic IVC: 24	_	—	DSS (5/10 year) Renal vein (51.5/39) IVC (33.4/0) Thrombus level (0.231. NS)
Staehler and Brkovic 2000	74	Level I: <5 cm above renal vein Level II: >5 cm above renal vein and below hepatic veins Level II:I above hepatic veins and below diaphragm Level IV: above diaphragm	Major complications: 28	8	5-year overall survival (no evidence of metastases) Level I: 38 Level II: 38 Level III: 30 Level IV: 0 With evidence of metastatic disease at presentation, median survival = 13 months
Libertino (unpublished data)	243	Renal vein: 87 IVC: 126 Atrium: 30	_	3	CSS (5/10 years) Renal vein: 50/50 IVC: 35/25 Atrium: 20/15 Thrombus level (P = .04)

Abbreviation: NS, not significant.

SUMMARY

The surgical resection of large renal tumors with associated tumor and bland thrombus within the IVC presents a challenge to the urological surgeon. Given the magnitude of many of these procedures, surgeons who have experience at tertiary centers are most adept in their management. The authors' clinical experience is one of the largest to date, and they hope this article serves as guide to physicians treating this unique population. They also commend their colleagues who have encouraged alternative techniques with equivalent outcomes that adhere to the principles of urologic oncology.

REFERENCES

- 1. Jemal A, Siegel R, Ward E, et al. Cancer statistics. CA Cancer J Clin 2007;57(1):43–66.
- Lipworth L, Tarone R, McLaughlin J. The epidemiology of renal cell carcinoma. J Urol 2006;176(6 Pt 1): 2353–8.
- Chow W, Devesa S, Waren J. Rising incidence of renal cell cancer in the United States. JAMA 1999; 281(17):1628–31.
- Jayson M, Sanders H. Increased incidence of serendipitously discovered renal cell carcinoma. Urology 1998;51(2):203–5.
- Marshall F, Dietrick D, Baumgartner W, et al. Surgical management of renal cell carcinoma with intracaval neoplastic extension above the hepatic veins. J Urol 1988;139(6):1166–72.
- Skinner DG, Pfister RF, Colvin R. Extension of renal cell carcinoma into the vena cava: the rationale for aggressive surgical management. J Urol 1972; 107(5):711–6.
- Neves R, Zincke H. Surgical treatment of renal cancer with vena cava extension. Br J Urol 1987;59(5): 390–5.
- Montie J, el Amnar R, Pontes J, et al. Renal cell carcinoma with inferior vena cava tumor thrombi. Surg Gynecol Obstet 1991;173(2):107–15.
- Swierzewski D, Swierzewski M, Libertino J. Radical nephrectomy in patients with renal cell carcinoma with venous, vena caval, and atrial extension. Am J Surg 1994;168(2):205–9.
- Emmott R, Hayne L, Katz I, et al. Prognosis of renal cell carcinoma with vena cava and renal vein involvement: an update. Am J Surg 1987;154(1): 49–53.
- Hatcher P, Anderson E, Paulson D, et al. Surgical management of renal cell carcinoma invading the vena cava. J Urol 1991;145(1):20–3.
- 12. Zini L, Destrieux-Garnier L, Leroy X, et al. Renal vein ostium wall invasion of renal cell carcinoma with an inferior vena cava tumor thrombus: prediction by

renal and vena caval vein diameters and prognostic significance. J Urol 2008;179(2):450–4.

- Belis J, Pae W, Rohner T, et al. Cardiovascular evaluation before circulatory arrest for removal of vena cava extension of renal carcinoma. J Urol 1989; 141(6):1302–7.
- Treiger B, Humphrey L, Peterson C, et al. Transesophageal echocardiography in renal cell carcinoma: an accurate diagnostic technique for intracaval neoplastic extension. J Urol 1991;145(6):1138–40.
- 15. Zielinski H, Szmigielski S, Petrovich Z. Comparison of preoperative embolization followed by radical nephrectomy with radical nephrectomy alone for renal cell carcinoma. Am J Clin Oncol 2000;23(1):6–12.
- Nakano H, Nihira H, Toge T. Treatment of renal cancer patients by transcatheter embolization and its effects on lymphocyte proliferative responses. J Urol 1983;130(1):24–7.
- Schwartz M, Smith E, Trost D, et al. Renal artery embolization: clinical indications and experience from over 100 cases. BJU Int 2006;99(4):881–6.
- Moinzadeh A, Libertino J. Prognostic significance of tumor thrombus level in patients with renal cell carcinoma and venous tumor thrombus extension. Is all T3b the same? J Urol 2004;171(2 Pt 1):598–601.
- Leibovich B, Cheville J, Lohse C, et al. Cancer specific survival for patients with pT3 renal cell carcinoma—can the 2002 Primary Tumor Classification be improved? J Urol 2005;173(3):716–9.
- Kim H, Zisman A, Han K, et al. Prognostic significance of venous thrombus in renal cell carcinoma. Are renal vein and inferior vena cava involvement different? J Urol 2004;171(2 Pt 1):588–91.
- Patard J, Kim H, Lam J, et al. Use of the University of California Los Angeles integrated staging system to predict survival in renal cell carcinoma: an international multicenter study. J Clin Oncol 2004;22(16):3316–22.
- Kattan M, Reuter V, Motzer R, et al. A postoperative prognostic nomogram for renal cell carcinoma. J Urol 2001;166(1):63–7.
- Frank I, Blute M, Cheville J, et al. An outcome prediction model for patients with clear cell renal cell carcinoma treated with radical nephrectomy based on tumor stage, size, grade and necrosis: the SSIGN score. J Urol 2002;168(6):2395–400.
- Canes D, Wotkowicz C, Vanni A, et al. Prognostic significance of tumor thrombus level and perinephric fat invasion: the debate continues for pT3 disease [abstract 713]. Atlanta (GA): AUA; 2006.
- Robson C, Churchill B, Anderson W. The results of radical nephrectomy for renal cell carcinoma. J Urol 1969;101:297–301.
- Wotkowicz C, Libertino J, Sorcini A, et al. Management of renal cell carcinoma with vena cava and atrial thrombus: minimal access vs median sternotomy with circulatory arrest. BJU Int 2006;98(2): 289–97.

- Svensson L, Crawford E, Hess K, et al. Deep hypothermia with circulatory arrest. Determinants of stroke and early mortality in 656 patients. J Thorac Cardiovasc Surg 1993;106(1):19–28.
- Fitzgerald J, Tripathy U, Svennson L, et al. Radical nephrectomy with vena caval thrombectomy using a minimal access approach for cardiopulmonary bypass. J Urol 1998;159(4):1292–3.
- Cosgrove D, Sabik J. Minimally invasive approach for aortic valve operations. Ann Thorac Surg 1996; 62(2):596–7.
- Svensson L, Libertino J, Sorcini A, et al. Minimal access right atrial exposure for tumor extensions into the inferior vena cava. J Thorac Cardiovasc Surg 2001;121(3):589–90.
- Foster R, Mahomed Y, Bihrle R, et al. Use of cavalatrial shunt for resection of caval tumor thrombus in renal cell carcinoma. J Urol 1988;140(6):1370–1.
- Burt M. Inferior vena caval involvement by renal cell carcinoma. Use of venovenous bypass as adjunct during resection. Urol Clin North Am 1991;18(3):437–44.
- Ciancio G, Livingstone A, Soloway M. Surgical management of renal cell carcinoma with tumor thrombus in the renal and inferior vena cava: the University of Miami experience in using liver transplantation techniques. Eur Urol 2007;51(4):988–94.
- Ciancio G, Vaidya A, Savoie M, et al. Management of renal cell carcinoma with level III thrombus in the inferior vena cava. J Urol 2002;168(4 Pt 1):1374–7.
- Ciancio G, Soloway M. Renal cell carcinoma with tumor thrombus extending above diaphragm: avoiding cardiopulmonary bypass. Urology 2005;66(2):266–70.
- D'Ancona CA, Petrucci O Jr, Otsuka R. Renal cell carcinoma with thrombus in the inferior vena cava: extracorporeal circulation and deep hypothermia without open-chest surgery. Int Braz J Urol 2005;31(1):49–50.
- Chowdury U, Mishra A, Seth A, et al. Novel techniques for tumor thrombectomy for renal cell carcinoma with intraatrial tumor thrombus. Ann Thorac Surg 2007;83(5):1731–6.
- Zini L, Haulon S, Leroy X, et al. Endoluminal occlusion of the inferior vena cava in renal cell carcinoma with retro- or suprahepatic caval thrombus. BJU Int 2006;97(6):1216–20.
- Kapoor A, Nguan C, Al-Shaiji T, et al. Laparoscopic management of advanced renal cell carcinoma with level I renal vein thrombus. Urology 2006;68(3):514–7.
- Varkarakis I, Bhayani S, Allaf M, et al. Laparoscopicassisted nephrectomy with inferior vena cava tumor thrombectomy: preliminary results. Urology 2004; 64(5):925–9.
- Meraney A, Gill I, Desai M, et al. Laparoscopic inferior vena cava and right atrial thrombectomy utilizing deep hypothermic circulatory arrest. J Endourol 2003;17(5):275–83.
- 42. Pruthi R, Angell S, Brooks J, et al. Partial nephrectomy and caval thrombectomy for renal

cell carcinoma in a solitary kidney with an accessory renal vein. BJU Int 1999;83(1):142–3.

- Angermeier K, Novick A, Streem S, et al. Nephronsparing surgery for renal cell carcinoma with venous involvement. J Urol 1990;144(6):1352–5.
- Sengupta S, Zincke H, Leibovich B, et al. Surgical treatment of stage pT3b renal cell carcinoma in solitary kidneys: a case series. BJU Int 2005;96(1):54–7.
- 45. Blute M, Boorjian S, Leibovich B, et al. Results of inferior vena caval interruption by Greenfield filter, ligation or resection during radical nephrectomy and tumor thrombectomy. J Urol 2007;178(2):440–5.
- Rabbani F, Hakimian P, Reuter V, et al. Renal vein or inferior vena caval extension in patients with renal cortical tumors: impact of tumor histology. J Urol 2004;172(3):1057–61.
- Boorjian S, Sengupta S, Blute M. Renal cell carcinoma: vena caval involvement. BJU Int 2007;99 (5 Pt B):1239–44.
- Flanigan RC, Mickisch G, Sylvester R, et al. Cytoreductive nephrectomy in patients with metastatic renal cancer: a combined analysis. J Urol 2004; 171(3):1071–6.
- Pantuck A, Belldegrun A, Figlin R. Nephrectomy and interleukin-2 for metastatic renal cell carcinoma. N Engl J Med 2001;345(23):1711–2.
- Barney J, Churchill E. Adenocarcinoma of the kidney with metastases to the lung: cured nephrectomy and lobectomy. J Urol 1939;42:269–76.
- Hofmann HS, Neef H, Krohe K, et al. Prognostic factors and survival after pulmonary resection of metastatic renal cell carcinoma. Eur Urol 2005;48:77–82.
- Assouad J, Petkova B, Berna P, et al. Renal cell carcinoma lung metastases surgery: pathologic findings and prognostic factors. Ann Thorac Surg 2007;84: 1114–20.
- Blute M, Leibovich B, Lohse C, et al. The Mayo Clinic experience with surgical management, complications and outcome for patients with renal cell carcinoma and venous tumor thrombus. BJU Int 2004;94:33–41.
- 54. Terakawa T, Miyake H, Takenaka A, et al. Clinical outcome of surgical management for patients with renal cell carcinoma involving the inferior vena cava. Int J Urol 2004;14:781–4.
- Klatte T, Pnatuck A, Riggs S, et al. Prognostic factors for renal cell carcinoma with tumor thrombus extension. J Urol 2007;178:1189–95.
- Parekh D, Cookson M, Chapman W, et al. Renal cell carcinoma with renal vein and inferior vena caval involvement: clinicopathological features, surgical techniques and outcomes. J Urol 2005; 173:1897–902.
- 57. Ficarra V, Righetti R, D'Amico, et al. Renal vein and vena cava involvement does not affect prognosis in patients with renal cell carcinoma. Oncology 2001;61:10–5.
- Staehler G, Brkovic D. The role of radical surgery for renal cell carcinoma with extension into the vena cava. J Urol 2000;163:1671–5.