Renal Cell Carcinoma with Tumor Thrombus: A Review of Relevant Anatomy and Surgical Techniques for the General Urologist

23

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23.1 Introduction

Renal cell carcinoma (RCC) is estimated to account for 4.1% of all new cancer diagnoses and 2.4% of all cancer deaths in 2020 according to the National Cancer Institute SEER database. This will likely total 73,000 new cases and 15,000 deaths [1]. RCC is one of the most lethal of the common cancers urologists will encounter with a 5-year relative survival of 75.2% [1]. Renal cell carcinoma is one of a small subset of malignancies that are associated with tumor thrombus formation, which is tumor extension into a blood vessel. An estimated 4–10% of patients with RCC will have some degree of tumor thrombus extending into the renal vein or inferior vena cava at the time of diagnosis [2]. Tumor thrombi change the staging of RCC and therefore are an important part of initial patient workup. It is known that such tumors are more aggressive with higher Fuhrman grades, N+ or M+ at time of surgery and have higher probability of recurrence with lower cancer-specific survival [3]. Aggressive surgical intervention with radical nephrectomy and thrombectomy can be performed with survival benefits. Therefore, a thorough

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understanding of the surgical anatomy and approaches for varying levels of RCC tumor thrombus is of utmost importance when treating these patients.

RCC tumor thrombi are classified according to the extent to which they invade the inferior vena cava. The Mayo Clinic RCC Tumor Thrombus Classification System divides tumor thrombi into four categories ranging from level one to level four.

Level zero thrombi are limited to the renal vein. Level one thrombi extend into the inferior vena cava but less than two centimeters above the renal vein orifice. Level two thrombi are more than two centimeters above the orifice but below the hepatic vein. Level three thrombi extend above the hepatic vein but below the diaphragm, and finally level four thrombi are above the diaphragm [4]. Classifying the level of the tumor thrombus becomes vitally important in surgical planning as it will dictate the surgical approach. Level zero thrombi may be amenable to simple renal vein ligation while level four can require thoracotomy and possible open heart surgery with coordination of many surgical teams.

Here we will review the anatomy associated with each level of tumor thrombus and attempt to construct an outline for surgical techniques that may be used. We aim to give a concise overview so that general urologists may use it to understand these potentially complicated cases.

23.2 Anatomy of the IVC and Tributaries Related to Renal Surgery

Adequate knowledge of the normal anatomy of the inferior vena cava, its tributaries relevant to renal surgery, and common variations is essential in minimizing adverse events associated with complex radical nephrectomies and thrombectomy. The inferior vena cava ascends along the anterolateral border of the vertebral column to the right of the abdominal aorta where it enters the thoracic cavity at the level of T8 through the vena caval foramen of the central tendon of the diaphragm.

It is sometimes accompanied by the phrenic nerve through its foramen [5]. Cases of left-sided IVC and bilateral IVCs have been reported and should be identified pre-operatively [6]. Other important relations include the duodenum and head of the pancreas anteriorly at the level of the kidney, the hepatoduodenal ligament anteriorly at the level of the liver, the right renal artery passing posteriorly, and the root of the mesentery and right gonadal artery anteriorly [7].

The IVC tributaries relevant to renal surgery and classification of invasion of thromboses include right and left renal veins, right suprarenal vein, hepatic veins, and right and left inferior phrenic veins [8]. The renal veins drain into the IVC laterally at the level of L2. Thromboses of the renal veins constitute a level zero invasion [4]. The right suprarenal vein empties into the IVC laterally and slightly superior to the right renal vein also at L2 [9]. It formed an anastomosis with an accessory hepatic vein before emptying into the IVC in 20% of 440 patients in a study performed by Omura et al. [10]. The accepted normal anatomy of hepatic drainage is that the left, middle, and right hepatic veins empty into the IVC at the level of T8 immediately before the IVC enters the thorax [9]. However, a study by Fang et al. found that 61% of 200 cadavers' middle and left hepatic veins combined to form a common trunk that then emptied into the IVC. Additionally, it was not uncommon for additional, accessory veins to be present [11]. The hepatic veins also separate levels one and two from level three thrombotic invasions. Lastly, the inferior phrenic veins travel along the inferior aspect of the diaphragm and empty into the IVC as the IVC enters the vena caval foramen at T8 [9].

They are also highly variant in their course. The right inferior phrenic vein emptied into the right hepatic vein in 8% of cadavers in a 2005 study by Loukas et al. The left inferior phrenic vein was more highly variable being found emptying into the IVC (37%), left suprarenal vein (25%), left renal vein (15%), and left hepatic vein (14%) [12].

The kidneys are typically drained solely by the renal veins. However, there are many clinically significant variations in course and anastomoses [13]. The right renal vein is typically shorter in length at 2–2.5 cm and less commonly has anastomoses as compared to the left renal vein, but it still drains the right suprarenal vein in 6% of cases and the ascending lumbar vein in 3% of cases.

The left renal vein is typically 8.5 cm in length and drains the left suprarenal vein and left gonadal vein. It also commonly has additional tributaries from lumbar veins or the ascending lumbar vein. As it courses medially towards the IVC, it passes anteriorly to the aorta and inferiorly to the superior mesenteric artery, which creates a possible site of constriction commonly leading to a left-sided varicocele. Invasion of RCC into the left renal vein can also cause a left-sided varicocele if it obstructs the drainage of the left gonadal vein [14]. Cases of right-sided varicoceles caused by RCC invasion into the right renal vein have also been reported [15]. Other common variations of renal veins include multiple renal veins and a circumaortic left renal vein.

23.3 Kidney and Liver Venous Drainage and Anatomy

As mentioned previously, the kidneys are drained solely by the renal veins, but can have variations in course and anatomy [13]. The renal venous system has what is called a "free anastomosis" system in place due to extensive collateral communication through venous collars around minor calyceal infundibula, which allows venous blood to communicate and flow freely throughout all segments of the kidney [13, 16]. Venous drainage in the kidney begins as the interlobular veins that progresses as the arcuate, interlobar, lobar, and segmental veins.

A group of segmental veins then unite to form a tributary that becomes the renal vein. Having a group of segmental veins uniting to form the renal vein allows for extensive collateral venous drainage of the kidney, and occlusion of a segmental venous branch will have little effect on venous outflow [16]. The right and left renal veins lie anterior to their respective renal arteries as they drain into the IVC. An important anatomical difference to consider between the renal veins is the fact that the right renal vein measures approximately 2 to 4 cm long while the left renal vein is 6 to 10 cm [16]. The left renal vein receives drainage superiorly from the left suprarenal (adrenal) vein and drainage inferiorly from the left gonadal (testicular or ovarian) vein. In approximately 75% of the population, the left renal vein has the possibility of also receiving additional tributaries that can be clinically significant in size and are highly variable [13]. These anatomical variants are important considerations due to possibility of avulsion during a surgical procedure. The left renal vein exits the kidney and travels medially traversing the angle formed between the superior mesenteric artery anteriorly and the aorta posteriorly. The left renal vein can be compressed between these two structures, known as nutcracker syndrome. The right renal vein differs from the left in its course as it travels towards the IVC, as well as the fact that it does not have extrarenal vessels join its course before it enters the IVC [13].

Large RCC tumor thrombi have the potential to extend cephalically to a subhepatic level interfering with venous drainage from the liver; therefore, knowledge of hepatic venous drainage proves important role. Hepatic venous blood is returned to the IVC via the hepatic veins.

There are three major hepatic veins: the right, middle (central), and left hepatic vein that pass in a posterosuperior direction through the liver to empty into the IVC which lies posterior to the surface of the liver [17]. A variable number of small, accessory veins run from the liver directly into the IVC below the level of the main hepatic veins [17]. During the course of radical nephrectomies with subdiaphragmatic or intrathoracic tumor thrombus, it may be necessary to use liver transplant techniques to mobilize the right lobe of the liver and access the retrohepatic vena cava [18]. Knowledge of the anatomical relationships among these short hepato-caval vessels is key to assure optimal vascular control and prevent uncontrolled bleeding.

23.4 Supra-Diaphragmatic Vena Cava Anatomical Relations

An important surgical consideration for RCC tumor extending into the inferior vena cava is control of the distal end of the tumor thrombus [19]. For surgical removal of tumor thrombi extending above the level of the diaphragm, the suptradiaphragmatic vena cava must be exposed. On average the length of the supradiaphragmatic IVC (from right atrial appendage to diaphragm) was 20.6 mm and width 28.7 mm [19]. Relevant vascular anatomy in relation to the supradiaphragmatic IVC includes the phrenic veins, diaphragmatic veins, and the right phrenic nerve. The diaphragmatic veins and their location for insertion into the supradiaphragmatic vena cava, as well as the phrenic veins and right phrenic nerve in relation to the supradiaphragmatic IVC are important surgical considerations. Different approaches have been elucidated to gain access to the supradiagphragmatic IVC when performing a thrombectomy. Careful consideration must be taken with the abdominal approach as to not transect any of the important vasculature encountered when dissecting the IVC from the diaphragm.

23.5 Key Retroperitoneal Anatomical Landmarks Relevant to Renal Surgery (Diaphragm, Cysterna Chili, Lymph Nodes, Pleura)

The cisterna chyli is a saccular lymphatic structure located at the L1-L2 vertebral body level in an area known as the retrocrural space, located just beneath the abdominal aorta [20].

The cisterna chyli receives lymphatic drainage from intestines and lower body structures and anastomoses with other lumbar and intestinal lymphatics as it continues in the cephalic direction as the thoracic duct [21, 22]. Anatomical variations of the cisterna chyli are highly prevalent, and complex variations can result in a plexus configuration as opposed to a single identifiable duct [22]. This is a large ductal system that carries a significant amount of lymphatic fluid, and inadvertent intraoperative injury to this structure could potentially lead to postoperative chylous fistuli, chylothoraces, and refractory chylous leakage.

Therefore, identification and preservation of the cisterna chyli is critical during RCC tumor thrombus removal and lymph node dissection.

23.6 Modern Imaging, Role of CT, MRI, and US in RCC with Vein Thrombus

Imaging plays a vital role in the management of RCC from diagnosis, to staging of disease, as well as assessment of response to medical or surgical therapy. Evaluation of the proximal extent, volume of tumor thrombus, and potential caval wall invasion are all necessary information for pre-operative planning considerations [23]. A clear pre-operative understanding of the tumor burden and thrombus may also direct the need for multidisciplinary surgical approaches [23]. Historically, Inferior Vena Cavography was used for the detection and evaluation of tumor thrombi, however, this procedure was limited by its invasive nature and procedural complications [23], Rossi 2018. Revolutions in imaging throughout the past decade have had a significant impact on the ability to manage kidney cancer; conversely, new surveillance protocols combined with serial imaging and advances in cross-sectional imaging have enhanced the ability to grade and stage kidney cancer [24]. With respect to RCC with venous thrombus, the imaging modality used must reliably identify any infra- or suprahepatic as well as intra-cardial extension of the thrombus [25]. Pre-operative determination of the tumor thrombus stage and the cranial extent of the thrombus is used to guide pre-operative planning for surgical approach to resection [25]. Different modalities that are currently used for pre-operative planning include MRI, CT, and ultrasound. CT remains the most appropriate imaging modality for classification of RCC thrombus. While RCC can appear as iso-, hyper-, and hypodense lesions on non-contrast CT, it usually demonstrates significant contrast enhancement and areas of necrosis following intravenous contrast application [25]. When compared to CT, MRI has superior soft tissue contrast resolution and ultrasound has found increasing utilization for repeated scanning and surveillance of tumors. While ultrasound is a non-invasive and commonly used way to evaluate patients with RCC, this method is largely dependent on the ultrasonographer and the position of the thrombus. It has been shown that the use of ultrasound to detect tumor thrombus location below the level of the insertion of the hepatic vein has a sensitivity of 68% [23]. Several studies have shown that a multiparametric imaging approach is most likely to yield the highest diagnostic accuracy [25]. While perioperative imaging for tumor thrombus removal is essential, intraoperative imaging can also be performed with transesophageal echocardiography (TEE), which gives the surgeon a real-time view of the tumor. The use of TEE has been studied and has proved effective as a technique to monitor the tumor thrombus position intra-operatively. This imaging modality is used most often as a way to delineate the uppermost rim of the tumor thrombus for higher stage tumors, such as those that extend into the atrium of the heart [26].

23.7 Surgical Approaches

After determining the level of tumor thrombus, the surgeon should begin to formulate a surgical plan. One of the first decisions the surgeon will make is the approach the he or she will take for the operation. This decision should not be overlooked as there are many described approaches and advantages and disadvantages to consider for each. Here we will discuss different incision types and the appropriate times for their use. The most commonly used incisions in renal surgery, including IVC thrombectomy, are flank, subcostal, midline, and thoracoabdominal.

The flank incision, while commonly used for access and exposure of the kidney and renal hilum in nephrectomies and partial nephrectomies may be inadequate in providing exposure to the IVC, thus, its utility in these operations is limited [23]. The subcostal incision is a popular approach as it gives excellent exposure to the renal hilum and the IVC. The incision can be extended laterally (chevron incision) in the case of bilateral disease and can also be extended superiorly for a sternotomy in the case of level IV thrombi. Subcostal incisions are associated with a high degree of postoperative pain [27]. The midline incision is an attractive approach for these complex surgeries as it also provides excellent IVC exposure as well as access to bilateral kidneys and renal hila. The midline incision can be extended cephalad for sternotomy. The disadvantage to this approach is that it may limit the ability to manipulate the liver and have access to the retrohepatic IVC should this be necessary [27]. The thoracoabdominal incision can also be considered. This incision may provide the best exposure to the hepatic vessels and retrohepatic IVC, however, this advantage must be balanced with the possible complications. These include severe post-operative pain, pneumothroax, phrenic nerve injury, impairing diaphragmatic function, splenic injury, as well as requirement of a chest tube post-operatively [28].

23.8 Liver Transplant Techniques

When a tumor thrombus extends into the inferior vena cava above the hepatic vessels (level III and IV tumor thrombus), liver transplant surgical techniques will likely need to be employed for proper control. Mobilization of the liver (Langenbuch maneuver) is necessary to obtain access to the retrohepatic IVC. This begins with dividing the triangular ligamentous attachments as well as the falciform ligament.

The small hepatic veins draining the caudate lobe are also ligated. This technique will allow for excellent visualization of the retrohepatic IVC [27]. Care must be taken to preserve the left, right, and middle hepatic veins as these are the primary venous drainage sources of the liver and cannot be sacrificed [29].

During liver mobilization, a Pringle maneuver may also be performed to decrease the amount of vascular congestion and bleeding from the liver. This is only necessary when a vascular clamp is placed above the hepatic vessels. In the pringle maneuver, the surgeon first identifies the Foramen of Winslow and then the hepatoduodenal ligament, which includes the hepatic artery, portal vein and the common bile duct. The hepatoduodenal ligament is then clamped.

Care must be taken to minimize the amount of time the hepatoduodenal ligament is clamped as splenic congestion, portal vein thrombosis, and ischemic liver injury can occur if the clamp times exceeds 60 min [30].

In some instances, tumors of the left kidney may require further exposure to the left retroperitoneum. To do this, the surgeon may perform the Mattox maneuver, which is commonly used in trauma surgery to control bleeding in the left retroperitoneum. Interestingly, this technique was first described by a chief surgery resident, Dr. Kenneth Mattox, working with a second year urology resident during a trauma case at Baylor College of Medicine. During the case, they needed to quickly mobilize the viscera to obtain access to the retroperitoneum as the patient was bleeding and the source was suspected to be either the aorta or IVC. Since that time, the maneuver has carried his name [31]. The maneuver begins by incising the peritoneum along the White Line of Toldt from the splenic flexure to the sigmoid colon. Once this is done, the spleen, tail of pancreas, left kidney, and the stomach may be mobilized.

23.9 Extracorporeal Circulation and Combined Cardiothoracic Approaches

When the IVC is completely occluded, a bypass mechanism must be used to ensure venous return to the heart. This has historically been done with two different methods: cardiopulmonary bypass (CPB) and venovenous bypass (VVB). If these techniques must be used, it is important to have assistance from a cardiothoracic surgeon and anesthesia team with experience in these cases. The level of extension of the tumor thrombus will dictate the bypass technique that is used. For level IV thrombi, a CPB will be necessary prior to atriotomy. During a CPB, the femoral vein and superior vena cava are cannulated as well as the right subclavian artery. An oxygenator is utilized to return oxygenated blood back to the arterial system.

The patient will require systemic heparinization as well as deep hypothermic circulatory arrest (DHCA), which allows the bypass circuit and heart to be stopped once hypothermia is achieved. CPB carries a high risk of stroke and perioperative mortality [27].

Venovenous bypass (VVB) can be used when the tumor thrombus extends above the diaphragm but not into the right atrium. During this procedure, the IVC is controlled above the level of the tumor thrombus, possible in the intracaval section, and the inferiorly below the renal veins. The IVC, or more commonly the femoral vein, is the cannulated as well as the SVC. This allows venous bypass around the clamped IVC.

23.10 Robotic RCC Thrombus Removal

As discussed in previous sections, traditionally surgery for renal cell carcinoma with tumor thrombus has been performed via an open approach requiring large thoracoabdominal incisions. However, in recent years there have been advances in the use of laparoscopic and robotic-assisted approaches for these complex cases, including level III thrombi. In 2000, Savage and Gill reported the first case report of a planned laparoscopic nephrectomy and tumor thrombectomy extending into the renal vein (level I thrombus) with good success [32]. Following this report, Desai et al. published a case series in 2003 showing the feasibility of a laparoscopic approach in patients with level I tumor thrombi [33]. In 2014, Shao et al. published a report of successful laparoscopic radical nephrectomy and thrombectomy in 11 patients with right-sided RCC, including six with level II thrombi and five with level IV thrombi. No major intraoperative or postoperative complications occurred showing the feasibility of a minimally invasive technique even in the most difficult patients.

Since that time, some major advancements have been made in the field of minimally invasive surgery including the widespread implementation of robotic-assisted laparoscopic surgery. Urologists were among the earliest adopters of robotic surgery and in 2000 the first procedure performed on the da Vinci system in the USA was a prostatectomy [34]. The robot has continued to be an important tool utilized in urologic procedures and is now commonplace in renal cancer surgery. In 2011, Abaza published the first case series involving robotic-assisted nephrectomy with tumor thrombectomy. In this series, five patients had this procedure with a mean operative time of 327 min, mean estimated blood loss of 170 cc, and mean length of stay of 1.2 days. The tumor thrombi extended into the IVC 1, 2, 4, and 5 cm as well as one patient that had two tumor thrombi extending 3 and 2 cm. The tumor thrombi extending 5 cm into the IVC reached the level of the liver, which would classify this as level III, however, this classification was not noted in the paper. There were no complications, transfusions or readmissions for these patients and all patients required opening of the IVC as well as either tangential clamp or cross clamp of the IVC [35]. In 2015, Gill et al. published the first case series reporting nine patients that underwent level III tumor thombectomy. They were able to perform the entire procedure, including intrahepatic IVC control, IVC repair, radical nephrectomy, retroperitoneal lymphadenectomy completely intracoporeal utilizing a 7-port technique. The median operative time was 4.9 h, average estimated blood loss was 375 cc, and average hospital stay was 4.5 days. There were no intraoperative complications and 1 Clavien 3b postoperative complication [36]. Other groups have been able to replicate this procedure with good outcomes [37] and it seems that the robot may be poised to play a bigger role in RCC with tumor thrombus in the coming years.

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