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RESEARCH ARTICLE

Renal Cell Carcinoma with Supradiaphragmatic Tumor Thrombus: Avoiding Sternotomy and Cardiopulmonary Bypass

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ABSTRACT

Renal cell carcinoma (RCC) accounts for 2-3% of all malignant disease in adults and has a propensity to infiltrate the surrounding adjacent structures with a biologic predisposition for vascular invasion. This tropism for the venous system facilitates propagation into the renal vein and inferior vena cava (IVC) in up to 25% of patients with RCC. Surgical resection remains the mainstay treatment for RCC with venous tumor thrombus (TT) extension and the only hope for a potential cure. Higher thrombus levels correlate with more advanced stages of disease and thus poorer survival rates. Although CPB with circulatory arrest has been successfully performed during resection of these tumors, its use remains controversial due to the risk of coagulopathy, platelet dysfunction, and central nervous system complications. Complete intraabdominal surgical excision of level III thrombi can be achieved without sternotomy and CPB by utilizing hepatic mobilization maneuvers. The purpose of this review is to provide an update on the surgical management of these difficult cases of RCC with supradiaphragmatic tumor thrombi, including a description of transplant-based techniques that avoid sternotomy and cardiopulmonary bypass (CPB), minimizing intra- and post-operative complications.

Keywords: renal cell carcinoma; tumor thrombus; nephrectomy; thrombectomy; cardiopulmonary bypass; sternotomy; surgical technique

INTRODUCTION

Renal cell carcinoma (RCC) represents 3% of all adult malignancies, with 30% of RCC diagnosed at locally advanced or metastatic stages of disease.^{1,2} A special form of locally advanced disease is the tumor thrombus (TT), a neoplastic extension of the tumor inside the vein due to the unique proclivity of RCC to involve vascular structures. TT commonly grows from the intrarenal veins, through the main renal vein, and up the inferior vena cava (IVC) and rarely, the right cardiac chambers. TT extension into the IVC occurs in up to 10% of cases of RCC, reaching up to the right atrium in about 1% of cases.¹⁻⁷

RCC is rather insensitive to classic chemo- or radiotherapy protocols, therefore surgery is the only therapeutic approach with curative intention. Overall survival rates of 68% at 5 years have been reported in the best surgical candidates (absence of distant metastatic spreading in cross-sectional imaging at debut); meaning that the presence of TT itself does not imply a worse prognosis.⁸ However, it seems reasonable that higher thrombus levels correlate with more advanced stages of disease and thus poorer survival rates.^{9,10} The objective of surgery is the complete removal of neoplastic tissue, including the intravascular component, which is often the most difficult part of the intervention. Complications are rather frequent and can be devastating, making the procedure a challenge for both the surgeon and patient.

The purpose of this review is to provide an update on the surgical management of these difficult cases of RCC with supradiaphragmatic tumor thrombi, including a description of specific techniques used to minimize intra- and post-operative complications by avoiding sternotomy and cardiopulmonary bypass (CPB).

Tumor thrombus anatomic level and classification systems

A crucial element in preoperative workup is to determine the level of the tumor thrombus. Many classification systems have been used in the last 50 years to classify these types of tumors, providing not only prognostic information but practical

information for surgical planning. The most commonly used classification system is the one described by Neves and Zincke.¹¹ As dealing with higher level thrombi become increasingly more complicated, authors at the University of Miami Miller School of Medicine¹² further expanded the classification for level III tumor thrombi to provide a clear depiction of the surgical maneuvers that should be used for each case. The authors subdivided level III thrombi into four groups: IIIa (retrohepatic IVC below major hepatic veins), IIIb (retrohepatic IVC reaching the ostia of major hepatic veins), IIIc (retrohepatic IVC and extending above major hepatic veins, but below diaphragm), and IIId (suprahepatic and supradiaphragmatic IVC, reaching intrapericardial IVC, but infra-atrial) (Figure 1).

Avoiding sternotomy and cardiopulmonary bypass (CPB)

A multidisciplinary approach is critically important in the treatment of RCC patients with supradiaphragmatic thrombi as resection of the tumor thrombus can lead to complications such as venous congestion, embolic events, and excessive blood loss^{13,14}. Complications depend mainly on the level of vascular involvement, venous redistribution in response to IVC, and the sequence of surgical steps performed.¹³⁻¹⁷

CPB with circulatory arrest has been successfully performed during resection of these tumors.¹⁸ Some authors prefer the use of CPB in efforts to decrease the risk of unexpected and life-threatening intraoperative hemorrhage and incomplete tumor excision,¹⁹ however, its use remains controversial due to the risk of renal failure, coagulopathy, platelet dysfunction, and central nervous system complications.^{20,21} Complete intraabdominal surgical excision of level III and IV thrombi can be achieved without the sternotomy and CPB by utilizing hepatic mobilization maneuvers.^{20,22-24}

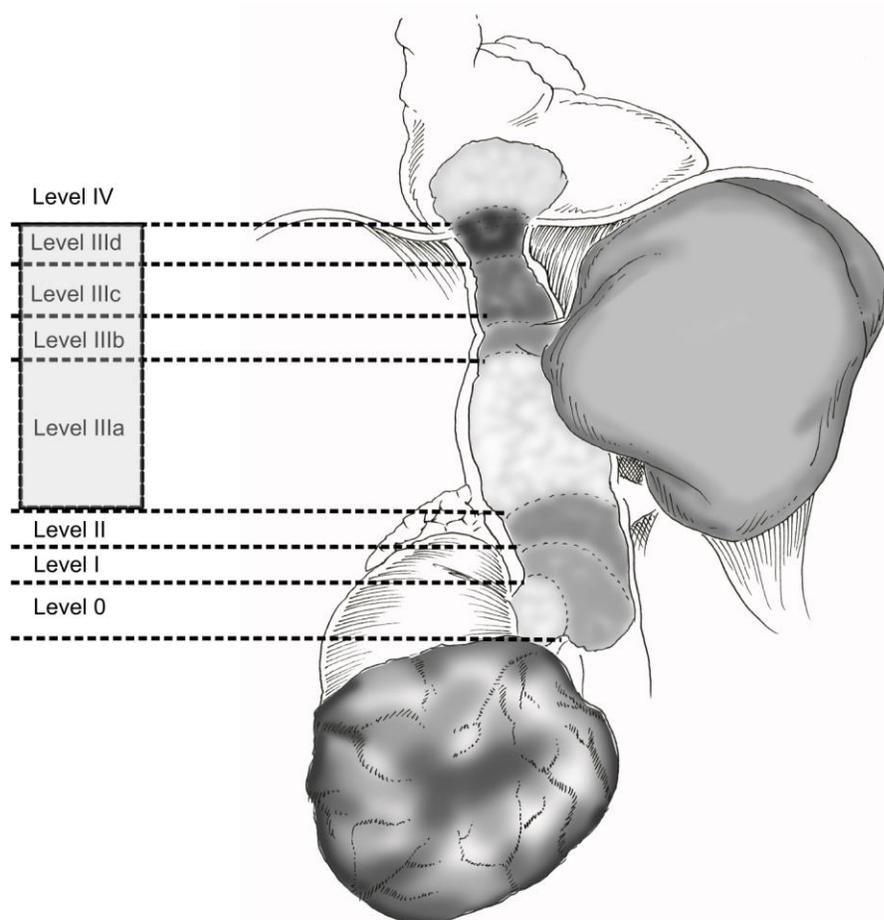


Figure 1. A combination of the Neves-Zincke and University of Miami Classification Systems for the tumor thrombus location inside the inferior vena cava lumen. The University of Miami Classification System is divided into four categories: IIIa (retrohepatic IVC below major hepatic veins), IIIb (retrohepatic IVC reaching the ostia of major hepatic veins), IIIc (retrohepatic IVC and extending above major hepatic veins, but below diaphragm), and IIId (suprahepatic and supradiaphragmatic IVC, reaching intrapericardial IVC, but infra-atrial).

In the case of level III tumor thrombi, Ciancio et al²² describe a transplant-based approach for gaining access to the retrohepatic IVC. The liver is mobilized by dissection and division of the ligamentum teres, followed by cautery division of the falciform ligament. The incision is then carried down to the right superior coronary and triangular ligaments. The visceral peritoneum overlying the right hepatic hilum and the infrahepatic IVC are then incised together with the right inferior coronary and hepatorenal ligaments. The liver can then be rolled to the left abdomen. Surgical control of the hepatic hilum is performed, permitting isolation and control of the porta hepatis to permit a Pringle maneuver when needed (if the thrombus extends above the hepatic veins).^{15,25} Then, a piggyback maneuver can be performed.²⁶ Minor hepatic veins draining into the anterior surface of the IVC are ligated and divided, allowing the infrahepatic, retrohepatic and suprahepatic portions of the IVC to be completely exposed. Finally, the posterior

surface of the IVC is completely dissected in order to obtain total circumferential dissection of the IVC.

If the TT can be milked down below the hepatic venous confluence, a clamp may be applied on IVC below the hepatic venous outflow, thereby avoiding liver congestion.²⁷ This step should be monitored with TEE to assess the level of the clamp and the potential dislodgement of the thrombus and possible subsequent pulmonary embolism. This milking maneuver (Figure 2) avoids hepatic dysfunction and preserves liver drainage into the IVC through the suprahepatic veins. This technique is often feasible, especially when early ligation of renal artery is performed as blood supply to the tumor thrombus is reduced. For level IIIc thrombi (suprahepatic and supradiaphragmatic IVC, reaching intrapericardial IVC, but infra-atrial), and for those cases where the milking maneuver is not feasible, dissection continues until the supradiaphragmatic and intrapericardial IVC is exposed. Intrapericardial IVC exposure requires the

opening of the central tendon of the diaphragm in the midline. After gaining complete circumferential control over the IVC at this level, gentle traction at the cavo-atrial junction permits the relocation of the right atrium inside the abdomen where it can be also controlled with vascular clamps.²⁸ Thrombectomy can then be performed after sequential vascular clamping as follows: i) IVC below the thrombus, ii) contralateral renal vein (and right adrenal vein in case of left-sided renal tumor), iii) Pringle maneuver, and iv) IVC above the TT (below the MHVs if milking maneuver was successful or supradiaphragmatic IVC if not). This vascular clamping is done with the help of TEE.^{21,25} However, the combination of flow interruption including the IVC and the liver circuit (Pringle maneuver) may

result in hemodynamic instability due to insufficient venous return. Thus, a test clamp is recommended prior to proceeding with cavotomy. In the case of significant hypotension, either rapid infusion (i.e., fluids or blood products) through a central line or bypass instauration (i.e., veno-venous or cardiopulmonary) is recommended.⁵ However, cardiac preload is commonly guaranteed through the natural liver bypass in partially occluding lower-level thrombi. Higher-level thrombi (level IIIb-IV) exhibit larger TT diameters, occasionally invading the IVC wall. In these later cases, collateralization is the rule favoring tolerance to the combination IVC cross-clamping and Pringle maneuver.

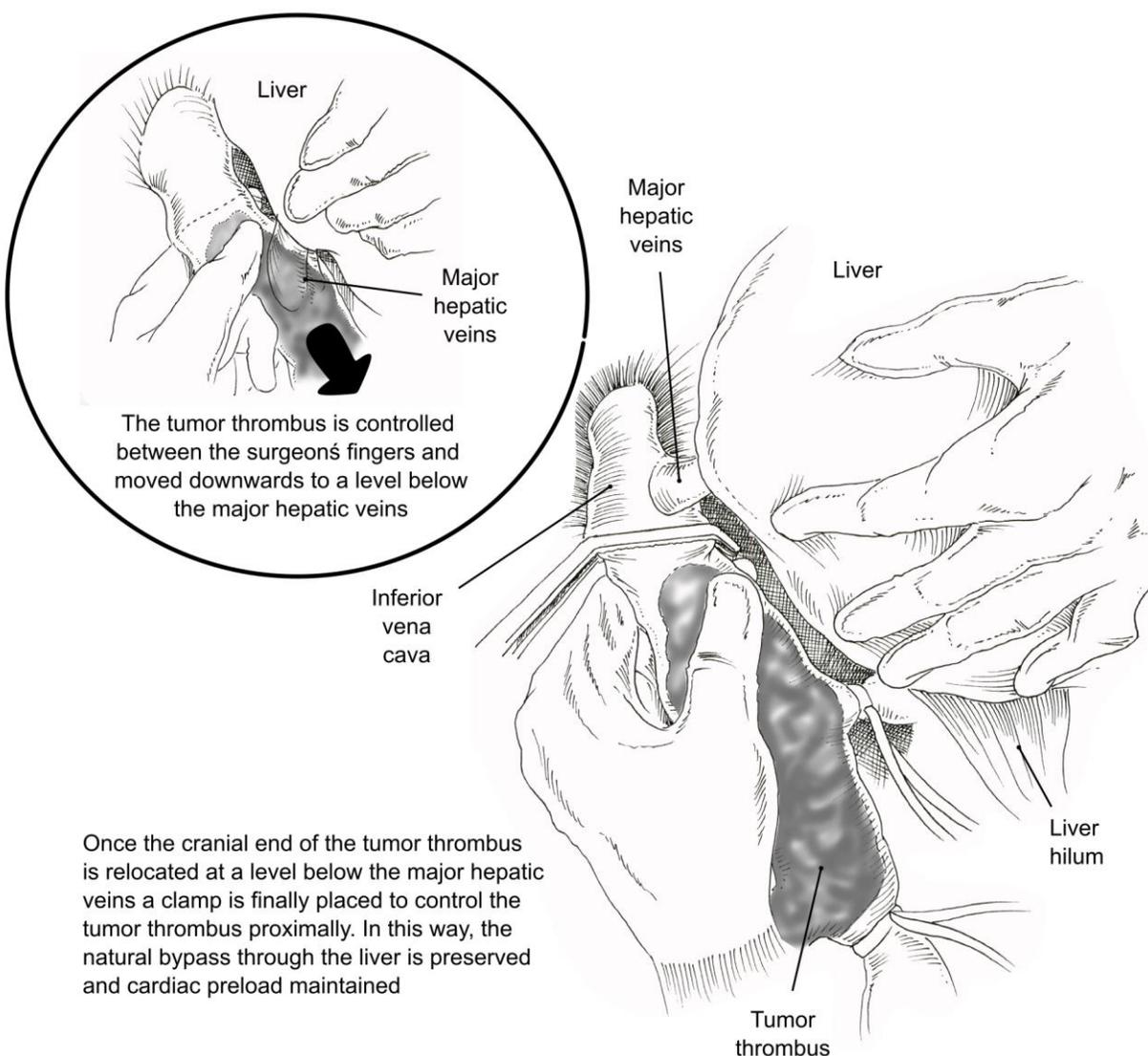


Figure 2. The milking maneuver.

The use of CPB with or without hypothermic circulatory arrest in management of level IV thrombi has been widely accepted.^{18,19} In cases of non-massive atrial involvement, right atrium control may be gained exclusively through the abdomen following the principles of the transplant-based approach described above, thus avoiding the need for sternotomy and CPB in most instances.²⁸

In a large observational study using the International Renal Cell Carcinoma-Venous Thrombus Consortium (IRCC-VTC), Gonzalez et al¹⁴ compared the clinical outcomes following radical nephrectomy and tumor thrombectomy utilizing a transplant-based (TB) approach vs. a non-transplant based (non-TB) approach in patients with RCC with level II-IV thrombi. The TB approach, which required CPB in 4.1% (4/98) of cases, was superior in limiting blood loss and the development of postoperative complications (PC) when compared to a non-TB approach that required CPB in 28.1% (82/292) of cases. The percentage who developed any PC (Clavien Grade 1-5) and PC categorized by minor (Clavien Grade 1-2) and major (Clavien Grade 3-5) grades were both significantly higher among those receiving the non-TB (vs. TB) approach, with 70.5% (206/292) vs. 15.3% (15/98) developing any PC, 49.3% (144/292) vs. 7.1% (7/98) developing a minor PC, and 21.2% (62/292) vs. 8.2% (8/98) developing a major PC, respectively.

Recent advances

In recent years, minimally invasive kidney cancer surgery for the management of radical nephrectomy and IVC tumor thrombectomy has been increasingly reported in the literature.²⁹⁻³⁴ Laparoscopic techniques for excision of locally invasive RCC have been described for over two decades, however its utilization for resection of higher level thrombi are considered challenging.³¹ Advances in robotic surgery and techniques have recently been applied to IVC thrombectomy.

Wang et al³⁵ proposed a robotic approach focused on the spatial relationship

between the TT cranial end and the location of the hepatic hilum and MHVs. This technique follows the surgical principles of the transplant-based approach, avoiding sternotomy and CPB.²⁵ For patients with level IIIa TT, the Pringle maneuver was not required. For cases of level IIIb-d TT, the liver was mobilized in a piggy-back fashion and the Pringle maneuver was established before clamping the suprahepatic segment of the IVC under TEE. Cases exhibiting complete caval occlusion with sufficient collateralization underwent IVC stapling with an endo-GIA. In 2019, the authors discuss their technique when confronted with a challenging scenario of level III-IV thrombi,³⁶ carefully selecting the candidate and excluding those cases in which caval invasion was anticipated. In the same way, they highlighted the importance of a multidisciplinary team in both preoperative planning and surgical intervention.

CONCLUSIONS

Renal cell carcinoma with vascular involvement remains a surgical challenge that has lasted for more than a century. Adequate classification of the anatomical level of the TT inside the IVC has made it possible to design surgical strategies personalized to each case, obviating the need of access to cavities other than the abdomen or auxiliary procedures such as CPB for safe and successful resection.

DECLARATIONS:

Conflicts of Interest Statement: The authors have no conflicts of interest to declare.

Authors contributions:

- (I) Conception and design: MMT, JG, GC
- (II) Administrative support: not required
- (III) Provision of study materials or patients: not applicable
- (IV) Collection and assembly of data: not required
- (V) Data analysis and interpretation: not required
- (VI) Manuscript writing: MMT, JG, GC
- (VII) Final approval of manuscript: MMT, JG, GC

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