En Bloc Resection of Right Renal Cell Carcinoma and Inferior Vena Cava with Tumor Thrombus: Is It Safe to Divide the Left Renal Vein?

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Abstract

Background

It has been suggested that IVC reconstruction of retroperitoneal tumors is not required when adequate collateral circulation is present, though transient rise in creatinine may occur post-operatively. There are no reports evaluating mid- and long-term effect on renal function in these patients. The purpose of this study is to assess whether resection of a right renal cell carcinoma and inferior vena cava with obstructing tumor thrombus is safe to perform without reconstructing the inferior vena cava with regard to long-term renal function.

Materials and Methods

A bi-institutional retrospective review was performed over an 18 year period, assessing patients with right renal cell carcinoma and obstructing level II-IV tumor thrombus.

Results

Twenty-two patients were included in the study. Median age was 62.5 (range 45-79) years old and 19 (86%) of the patients were male. One patient (5%) had a level II thrombus, 14 patients (64%) had a level III thrombus (IIIa n=3, IIIb n=6, IIIc n= 3, IIId n=2), and seven patients (32%) had a level IV thrombus. Intra-operatively, median estimated blood loss was 1.35 (range 0.2 – 25) L. The median length of hospital stay was 11 (range 5 – 50) days. Median preoperative creatinine was 1.20 (range 0.40 – 2.70) mg/dL and postoperatively, median creatinine was 1.3 (range 0.86 – 2.20) mg/dL. Median creatinine at 6 month and 12 months follow-up was 1.10 (range 0.5 – 1.6) and mg/dL 1.34 (range 0.6 – 2.0), respectively. Eight patients were lost to follow-up, and two died (one in the hospital, and the other three months post-operatively).

Conclusions

Resection of right renal cell carcinoma with inferior vena cava in the presence of an obstructing level II- IV tumor thrombus without reconstruction of the inferior vena cava appears not to have a significant adverse effect on long-term renal function.

I. Background

Renal cell carcinoma (RCC) infrequently extends into the renal vein and inferior vena cava (IVC) in the form of a tumor thrombus (TT).[1,2] When it does, surgical resection is the mainstay in treatment of this complex tumor to aid in oncologic control and/or symptomatic palliation.[3,4] As the TT grows, it gradually

occludes the IVC lumen, provoking a redistribution of venous blood flow through pre-existing connections between the IVC and lumbar and azygos-hemiazygos venous plexuses.[5–7] These collaterals allow cardiac preload to remain unaltered in response to IVC occlusion.

A few case reports of retroperitoneal masses including sarcomas, Wilms tumor, RCC, and testicular tumors with TT and IVC obstruction necessitating IVC resection have suggested that IVC reconstruction is not required when adequate collateral circulation is present, though transient rise in creatinine may occur post-operatively.[8–10] This may be the result of hemodynamic changes or volume depletion during surgery, in which case improvement is expected over days to weeks after surgery. There are no reports evaluating mid- and long-term effect on renal function in these patients. The objective of this study is to assess the impact of right radical nephrectomy for RCC with en bloc resection of the IVC and TT without caval reconstruction on post-operative renal function.

Ii. Methods And Patients

A bi-institutional retrospective review was performed for patients undergoing right radical nephrectomy and en bloc resection of IVC and TT between 2006 and 2021. Only patients with obstructing thrombus levels II-IV were included. Cranial extent of tumor was defined per our own classification for level III[11], and the classification by Neves and Zincke was used for level II and IV thrombus.[12] Level III thrombi were classified as level IIIa (retrohepatic), level IIIb (hepatic), level IIIc (suprahepatic, infradiaphragmatic), or level IIId (supradiaphragmatic, infra-atrial) (Figure 1).[11]

After extensive evaluation and cardiology clearance, informed consent was obtained for right radical nephrectomy and thrombectomy with or without IVC reconstruction with possible cardiopulmonary bypass (CPB). CPB was planned in advance for cases of level IV thrombus with a large intra-atrial component, although the cardiothoracic team was on standby for all cases. Data collected included patient demographics; tumor characteristics including size, TT level, pathology, grade, and stage; intra-operative factors such as estimated blood loss (EBL), blood transfusions, use of CPB; complications; length of stay; and survival. Pre-operative creatinine was recorded, as was creatinine on day of discharge, and at 6 and 12 month follow-up. When creatinine result was not available for the exact follow-up time point (6 or 12 months), the value at the time closest to the intended time was used, so long as it was in a 3 month window (thus for 6 month follow-up, 3-9 month creatinine could be included, and 9-15 month creatinine for 12 month follow-up). All procedures described in this report were in accordance with the ethical standards of the University of Miami Miller School of Medicine and Hospital General Universitario Gregorio Marañón Institutional Review Boards and the Helsinki Declaration (as revised in 2013)

Surgical Technique

Following the technique previously described by Ciancio et al.,[1–3,11,13] a modified Chevron or J-shaped Makuuchi incision were used to gain abdominal access. A liver surgery self-retaining retractor (Rochard or

Omni-Tract®) was used in every case to create enough space at the level of diaphragmatic domes to further facilitate the approach to the suprahepatic segment of the IVC.

The right renal artery was identified, ligated and divided by creating a posterior plane of dissection or at the level of inter-aortocaval sulcus.[13] After its division, the collateral venous circulation collapsed, making the remaining dissection easier to perform. The liver was completely mobilized off of the IVC, with the only remaining structural attachments being the major hepatic veins (Piggyback liver mobilization) and the liver hilum.[1–3, 13] A plane was then created between the IVC and posterior abdominal wall to obtain circumferential control of the IVC. At this level, the engorged small tributaries (often confused for lumbar vessels) needed to be properly identified and ligated to prevent significant bleeding and to facilitate stapling of the IVC.

If TT extended to or above the diaphragm, the central tendon of the diaphragm was dissected to the supra-diaphragmatic area, until the intra-pericardial IVC was fully exposed (Figure 2). The dissection was circumferential so that the intra-pericardial IVC could be completely encircled below or above the confluence into the right atrium (RA). The RA was gently pulled beneath the diaphragm and into the abdomen. If more exposure of the RA was required, the central tendon of the diaphragm could be incised at the midline, allowing the pericardium to be exposed, and a pericardiotomy could be performed. Use of intra-operative transesophageal echocardiography (TEE) was critical to delineate the cranial extent and mobility of the tumor thrombus during dissection of the retrohepatic IVC, supra-diaphragmatic IVC and RA, and to confirm that there were no pulmonary artery emboli or TT extending into the RA. In addition, the intra-operative TEE acted as a guide during application of the vascular clamp onto the RA (if needed for proximal control due to extent of TT), making sure that the clamp excluded tumor and that the coronary sinus was not obstructed.

In cases of level IV thrombi with large intra-atrial component not fully accessible from the abdominal field, the use of CPB was considered necessary and planned in advance. For this purpose, a midline sternum incision was used. Cannulation was performed in a standard fashion through the right atrium, right femoral vein, and distal ascending aorta (Figure 3). Proximal aortic clamping and additional cannulation was used for plegic solution administration when required. The type and parameters of CPB utilized was discretional upon the criteria of the cardiothoracic team involved and do not represent a constant along the study period since a historical series is reported. Overall, CPB shifted from deep hypothermic under cardiac arrest to normothermic beating heart during the study period.

Once the liver and IVC were completely mobilized via the Piggyback technique, vascular clamps were placed in the infra-renal IVC, followed by the left renal vein. The TT was then milked below the major hepatic veins, and the IVC was clamped without the need of Pringle maneuver. If the TT was bulky, not freely mobile, and could not be milked downward out of the intra-pericardial IVC, Pringle maneuver was performed to temporarily occlude blood inflow to the liver. For level IV thrombi requiring bypass, thrombus was removed through a RA incision performed after CBP was initiated. Once the bulky atrial component was removed, the remaining proximal thrombus was pushed downwards and removed through the

cavotomy, ensuring complete thrombus removal and full patency of the major hepatic veins ostia. The cavotomy was sutured closed in its proximal segment and the IVC was stapled just below the major hepatic veins, and distal to the tumor thrombus caudal end (Figure 4). The left renal vein was either stapled or oversewed. At the end of the resection, TEE was repeated to rule out any pulmonary artery emboli or piece of TT left behind.

Iii. Results

Twenty-two patients were included in the study. Patients' demographics, tumor and thrombus characteristics, and perioperative variables are described in Table 1. Median age was 62.5 (range 45-79) years old and 19 (86%) of the patients were male. A majority of patients (N=14, 64%) had a level III thrombus (IIIa n=3, IIIb n=6, IIIc n= 3, IIId n=2). Seven patients (32%) had a level IV thrombus, and one patient (5%) had a level II thrombus. Median tumor size was 12 (range 4-27) cm. Intraoperatively, median estimated blood loss was approximately 1.35 (range 0.2–25) L, and patients were transfused a median of 3 (range 0 – 30) units of packed red blood cells. Surgery was completed without cardiopulmonary bypass (CPB) in 18 (82%) of the cases. For patients requiring CPB, two (9%) had an intra-operative cardiac arrest, while two (9%) did not have cardiac arrest. All patients requiring CPB had a level IV tumor thrombus. Median length of stay was 11 days but ranged from 5-50 days within the cohort.

Table 1
Patient demographics, tumor characteristics, and perioperative factors

All	**22 (100%)**
Sex	
Male	19 (86%)
Female	3 (14%)
Age (years)	
Median (min, max)	62.5 (45-79)
Thrombus level	
II	1 (5%)
III	14 (64%)
IIIa	3 (14%)
IIIb	6 (27%)
IIIc	3 (14%)
IIId	2 (9%)
IV	7 (32%)
Tumor size (cm)	
Median (min, max)	12 (4, 22)
Estimated blood loss (mL)	
Median (min, max)	1350 (200, 25000)
Units of packed red blood cells transfused	
Median (min, max)	3 (0 – 30)
Cardiopulmonary bypass (CPB) performed	
No	18 (82%)
Yes	4 (18%)
Pathology	
Clear cell	18 (82%)
Papillary	2 (9%)
Mixed	2 (9%)

All	**22 (100%)**
Stage	
Pathologic T stage	
T3b	12 (55%)
T3c	10 (46%)
Pathologic N stage	
N0	8 (36%)
N1	7 (32%)
N2	2 (9%)
Nx	5 (23%)
Clinical M stage	
M0	4 (18%)
M1	6 (27%)
Mx	12 (55%)
Length of stay (days)	
Median (min, max)	11 (5, 50)
Complications (Clavien-Dindo grade)	
0	9 (41%)
I	2 (9%)
II	8 (36%)
IIIa	1 (5%)
IIIb	0 (0%)
IVa	1 (5%)
IVb	1 (5%)

Tumor characteristics are also outlined in Table 1. A majority of patients had clear cell RCC (N=18, 82%), two patients (9%) had papillary RCC, and two patients (9%) had mixed cell pathology. Five patients (28%) had clear cell with differentiation. Of those, two patients had rhabdoid differentiation, two patients had sarcomatoid differentiation, and one patient had rhabdoid and sarcomatoid differentiation. Tumor staging and nodal metastasis are also described in Table 1. Twelve patients (55%) were classified as TMN stage T3b, and 10 patients (46%) were TMN stage T3c. Eight patients (36%) had no nodal

metastasis on pathology, while 9 patients (41%) had Stage 1 or 2 nodal metastasis, and 5 patients (23%) had nodal metastasis of unknown stage.

Clavien-Dindo grade of post-operative complications are presented in Table 1. Complications were observed in 13 (59%) of cases, 10 (77%) of which were Clavien-Dindo grade I-II. Of the remaining three cases, one patient had a grade IIIa complication, requiring chest tube placement under local anesthesia for a pleural effusion. Another patient with level IV tumor thrombus suffered a grade IVa complication including post-operative bleeding from the duodenum requiring reintervention for hemostasis, *C. difficile* infection, sepsis, and prolonged intensive care unit stay. Finally, in another case of a level IV tumor thrombus, the patient suffered a grade IVb complication with cardiogenic shock and death 44 days after surgery that required CPB, which was preceded by post-operative evisceration requiring abdominal wall repair with mesh plus pneumonia.

Median preoperative creatinine was 1.2 (range 0.4 – 2.7) mg/dL (Table 2). This tended to increase after surgery, with a median post-operative creatinine of 1.3 (0.9 – 2.2) mg/dL. Eight patients did not have follow-up creatinine available, and two patients died (one in the hospital, and the other three months post-operatively due to disease progression). Ten patients had a creatinine result available at 6 months post-op (Table 2). Median creatinine at 6 month follow-up was 1.10 (range 0.5 – 1.6) mg/dL. Creatinine at 12-month follow-up was available for six patients (3 of whom also had 6 month creatinine result available), with median 1.3 (range 0.6 – 2.0). No patients required renal replacement therapy at last follow-up.

Table 2
Perioperative creatinine trends

Pre-operative creatinine (mg/dL)		**N (missing)**
Median (min, max)	1.2 (0.4, 2.7)	20 (2)
Discharge creatinine		
Median (min, max)	1.3 (0.9, 2.2)	22 (0)
Creatinine at 6 months post-op		
Median (min, max)	1.1 (0.5, 1.6)	10 (12)
Creatinine at 12 months post-op		
Median (min, max)	1.3 (0.6, 2.0)	6 (16)

Iv. Discussion

Renal cell carcinoma with tumor thrombus extending to the intrahepatic IVC or the right atrium are technically challenging surgical cases, though complete resection remains a mainstay of treatment to improve overall survival.[1–4, 14] When performing right radical nephrectomy and IVC thrombectomy with a level II-IV obstructing tumor thrombus, this review demonstrates that ligation of the left renal vein may

safely be performed without adversely impacting renal function. Preserved renal function is demonstrated both in the immediate post-operative period and during follow-up, allowing patients to avoid renal replacement therapy and potential complications associated with IVC reconstruction.

While the right renal vein rarely develops adequate collaterals to redistribute venous return, the left renal vein develops sufficient collateral drainage in the setting of longstanding obstruction of the IVC through the left gonadal and adrenal veins, azygos-hemiazygos system, and occasionally through lumbar veins (which may be present on the posterior aspect of the left renal vein).[5–7, 14,15] Of note, ligation of the right renal vein is generally not safe because sufficient collateral drainage does not develop. Division of the left renal vein in the absence of adequate collateral drainage can result in impairment of renal function post-operatively (such as in abdominal aortic aneurysm repair).[16,17] Adequate collateral drainage and extensive bland thrombus can be identified on pre-operative imaging, and patients are not expected to have lower extremity edema on examination.[7,18,19] When it is unclear if adequate collateral drainage is present, it has been suggested that a clamp trial may be performed intra-operatively before division of the left renal vein. Tense engorgement within 3 minutes of clamping may indicate insufficient collateral drainage.[16]

This surgical approach represents a safe option which may also be used when using a robotic-assisted approach.[20,21] It simplifies the procedure since diversion of left renal vein into another vessel (such as the inferior mesenteric vein) or IVC reconstruction through grafting are not required,[15] thus avoiding operative time-consuming procedures and the need for prolonged antibiotic and anticoagulation therapy to prevent graft infection and/or occlusion (particularly frequent in the setting of hypercoagulability of malignancy).[15,22]

Although this is the largest experience available to date in the literature for circumferential IVC resection without reconstruction for right-sided RCC with level II-IV tumor thrombus, these cases remain rare even in referral centers, limiting sample size. Pre-operative creatinine was not available for two patients who underwent surgery before implementation of an electronic medical record. Since many of these patients are referred to a tertiary center for surgery, post-operative creatinine was not always available since some patients follow up at their home institution. This series includes patients from two centers where the surgical approach has been standardized. Nevertheless, the outcomes reported have to be handled cautiously since they may not be reproducible by surgical teams of different volume and experience.

V. Conclusions

For patients with right-sided renal cell carcinoma with obstructing level II-IV IVC thrombus, ligation of the left renal vein and resection of the IVC without reconstruction does not appear to adversely impact long-term renal function.

Declarations

Ethics approval and consent to participate: The Human Subject Research Office (HSRO) provides administrative support for the University of Miami Institutional Review Boards (IRB). This study (20200791) was approved by the University of Miami Institutional Review Board and abides by the Helsinki Declaration (as revised in 2013). The University of Miami IRB's decision to waive consent to participate required that the IRB find and document that: 1) The research involves no more than minimal risk to the subjects; 2) The waiver or alteration will not adversely affect the rights and welfare of the subjects; 3) The research could not practicably be carried out without the wavier or alteration; and 4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Consent for publication: Not applicable.

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Competing interests: The authors decplare that they have no competing interests.

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Authors' contributions: Conception and design: GC; Aqcuisition of Data: GC, LH, MRC, FHA, CH; Analysis and interpretation of data: JG, LH, JJG, GC; Writing of the manuscript: LH, MMT, RS; Statistical analysis: JJG; Supervision: GC, JJG

Ackonowledgements: Not applicable.

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Figures

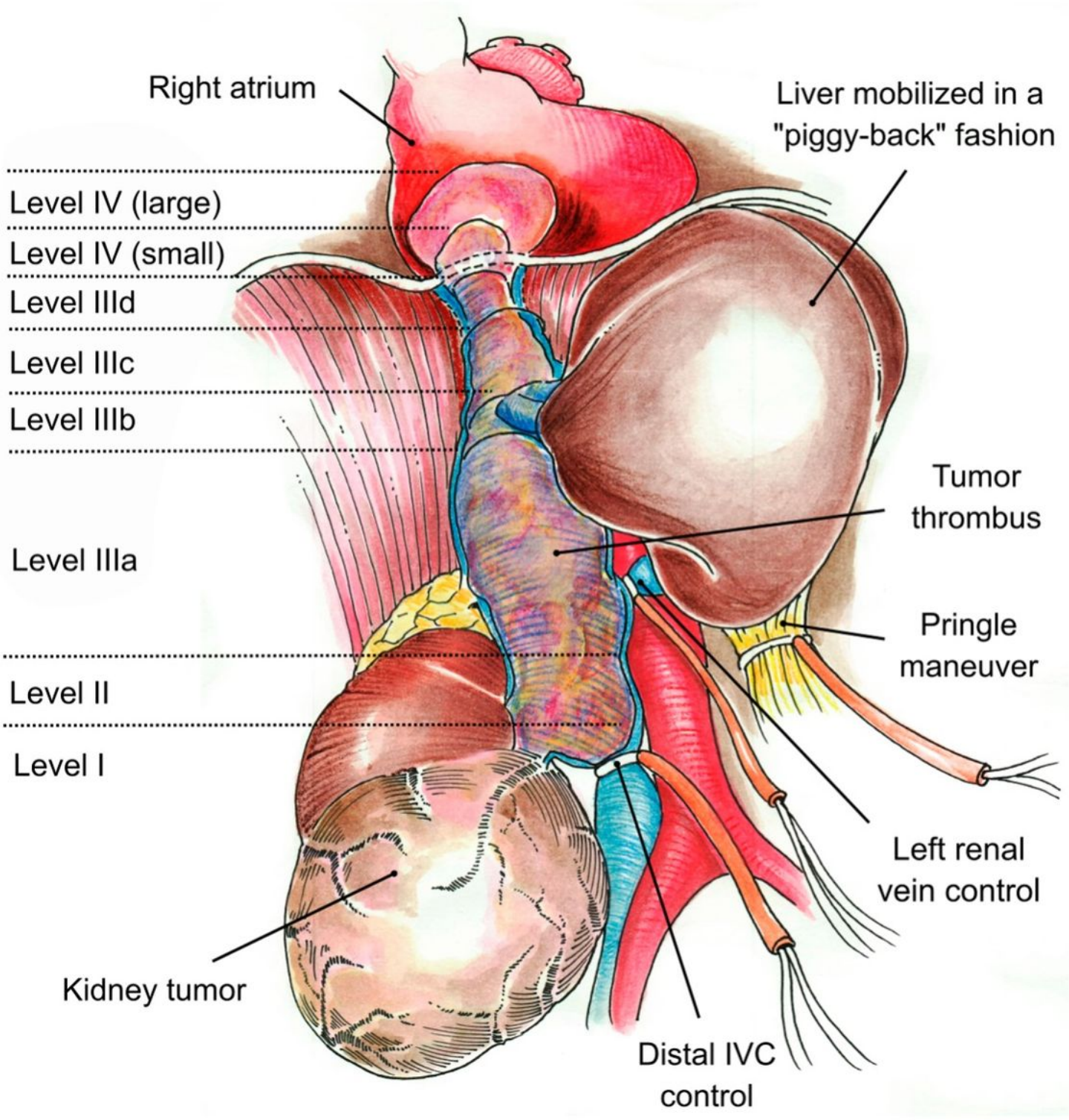

Figure 1

Neves and Zincke Classification System was used for level II and IV thrombus. Level III thrombi were classified as level IIIa (retrohepatic), level IIIb (hepatic), level IIIc (suprahepatic, infradiaphragmatic), or level IIId (supradiaphragmatic, infra-atrial).

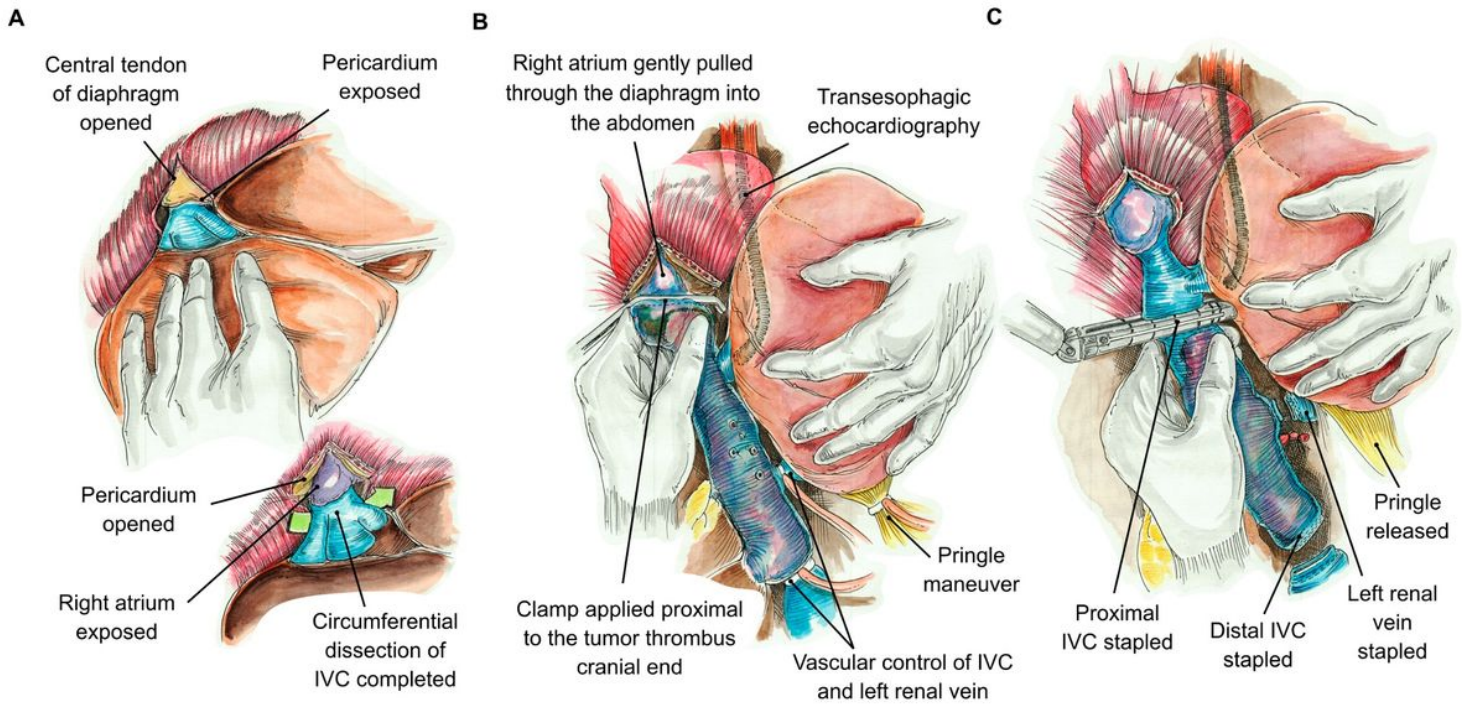

Figure 2

Tumor thrombus removal avoiding the use of cardiopulmonary bypass. The central tendon of the diaphragm is opened vertically and the pericardium exposed. If more exposure is required the pericardium may be also opened. Circumferential control of the inferior vena cava at a suprahepatic level facilitates tumor thrombus removal (A). The right atrium may be pulled downwards through the diaphragm and into the abdomen, and the cranial end of the tumor thrombus controlled under Pringle maneuver conditions by cross-clamping the inferior vena cava above this level. Simultaneous transesophagic echocardiography provides visual guidance during the performance of these maneuvers (B). When the tumor thrombus can be milked down distal to the major hepatic veins orifices, an endo-GIA stapler may be utilized to staple the inferior vena cava proximally. Once the inferior vena cava is stapled, the liver vascular flow can be reestablished by releasing the Pringle maneuver. The procedure is completed by stapling the inferior vena cava distally, and the left renal vein close to its entrance in the vena cava (C).

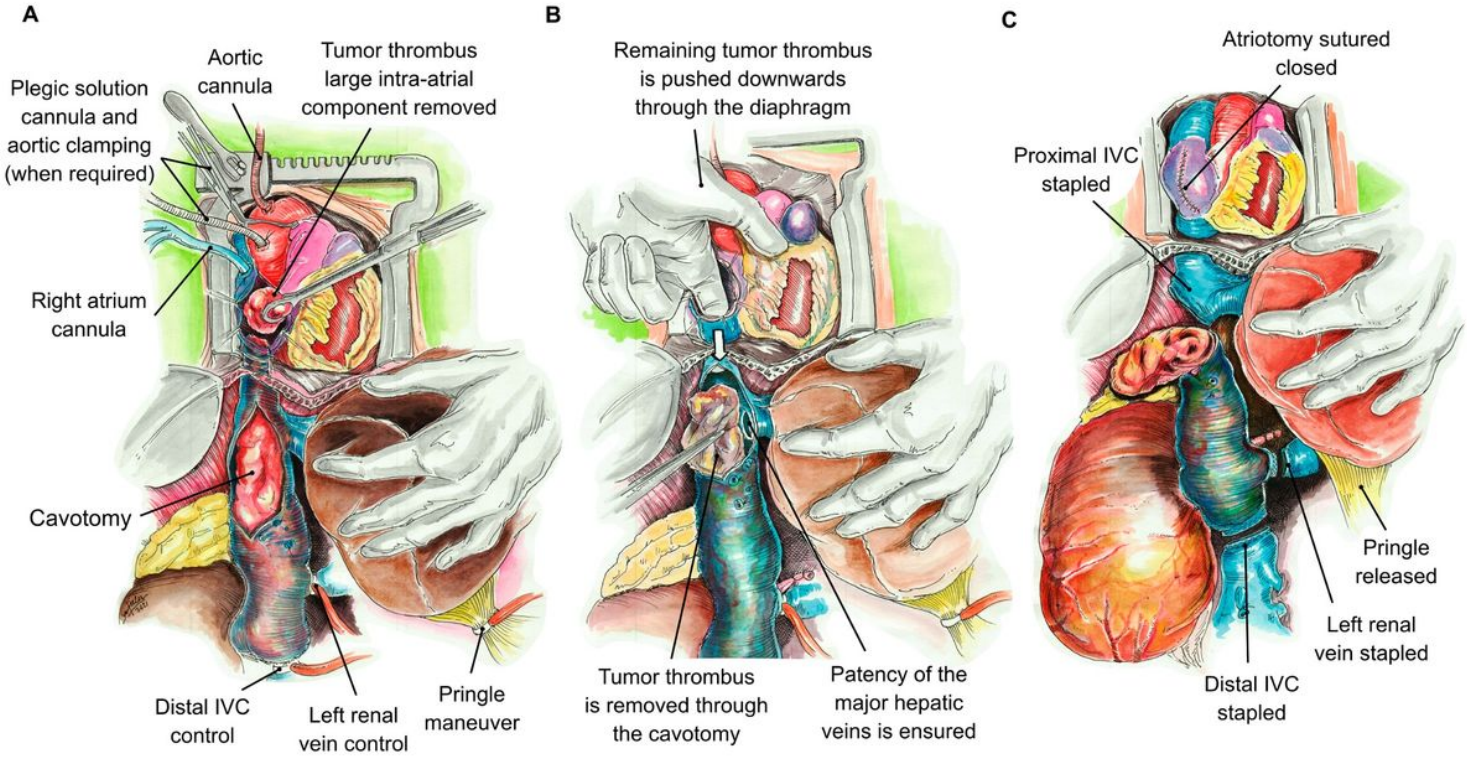

Figure 3

Tumor thrombus removal by means of cardiopulmonary bypass. Cannulae are placed in the aortic root and the right atrium. If cardiac arrest is required a vascular clamp is placed at the aortic arch proximally, and an additional cannula placed for plegic solution release. Pringle maneuver is initiated, a right atriotomy performed, and the large component of the tumor thrombus occupying the right atrium is removed through the atriotomy (A). The remaining tumor thrombus in the right atrium and proximal inferior vena cava is pushed downwards through the atriotomy in caudal direction. A longitudinal cavotomy permits the removal of the remaining tumor thrombus under direct visual control, ensuring the patency of the major hepatic veins ostia at the same time (B). Once the cranial thrombus component is removed, the inferior vena cava is stapled below the entrance of the major hepatic veins, the atriotomy is sutured closed, and the Pringle maneuver released to reestablish the vascular flow into the liver. The procedure is completed by stapling the inferior vena cava distally, and the left renal vein close to its ostium (C).

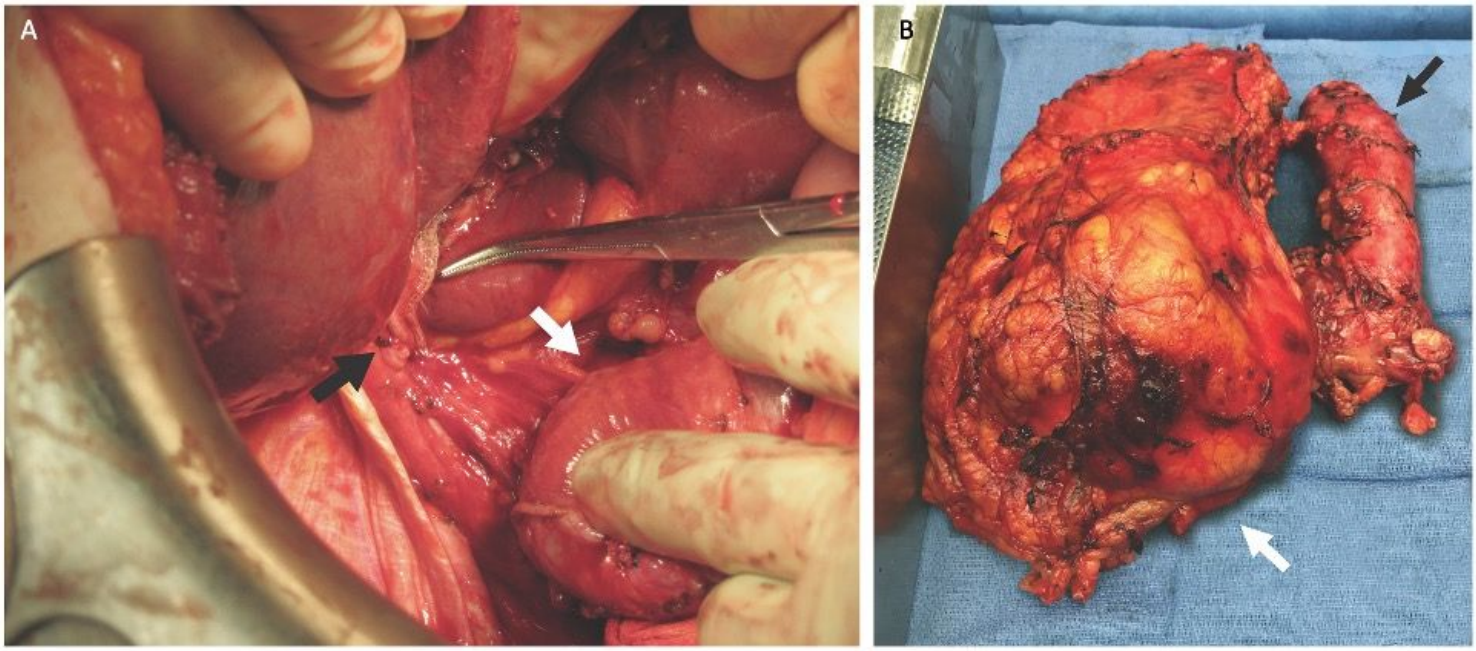

Figure 4

The Inferior Vena Cava (IVC) was stapled at the level of the major hepatic veins (black arrow). The IVC with tumor thrombus (TT) is under the surgeon hand (white arrow) (A). Surgical specimen of large right renal tumor (white arrow) with the IVC complete stapled containing the TT (black arrow) (B).