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# Surgical treatment of renal tumor with tumor thrombus in the *inferior vena cava*

## Hirurško lečenje tumora bubrega sa tumorskim trombom u donjoj šupljoj veni

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**Abstract**

**Background/Aim.** An aggressive approach with radical nephrectomy and thrombectomy is the mainstay of the treatment in patients with renal tumors. The aim of this study was to present the results of such surgical procedures performed in the last 25 years at our institution. **Methods.** We made a retrospective analysis of radical nephrectomy and thrombectomy in patients with renal tumor and tumor thrombus (TT) extending into the *inferior vena cava* (IVC) operated on at our institution between January 1995 and October 2021. **Results**. There were 92 patients (72 males and 20 females) aged 60.5 on average who were operated on in the mentioned period. A predominance of right-sided tumors was present in 73.33% of patients. Patients with TT in the renal vein (levels 0 and I) were not included. TT levels II, III, and IV were present in 32 (34.8%), 52 (56.5%), and 8 (8.7%) patients, respectively. One patient had thrombosis of the right pulmonary artery. Four patients had liver metastases, and ten had lymph node involvement. The surgical approach by subcostal incision was achieved in 8 (8.69%) patients, by chevron incision in only 11 (11.95%) patients, while in 73 (79.34%) patients, we performed median sternotomy and subcostal/chevron incision. Intraoperatively, there was one complication which was pulmonary thromboembolism. Six patient required re-exploration after the surgery due to the IVC hemorrhage. The three-year survival in patients with renal tumors and TT levels II–IV in the IVC was 43%. **Conclusion**. Surgery will remain the primary cure method in patients with renal tumors and TT in the IVC. Long-term survival in these patients can be achieved by complete surgical removal (radical nephrectomy and thrombectomy).

**Key words:**
**kidney neoplasms; neoplasm metastasis; vena cava, inferior; surgical procedures, operative; survival.**

**Apstrakt**

**Uvod/Cilj**. Agresivan pristup sa radikalnom nefrektomijom i trombektomijom je osnova lečenja bolesnika sa tumorom bubrega. Cilj rada bio je da se prikažu rezultati takvih hirurških zahvata, sprovedenih tokom poslednjih 25 godina u našoj ustanovi. **Metode.** Izvršena je retrospektivna analiza radikalne nefrektomije i trombektomije kod bolesnika sa tumorom bubrega i tumorskim trombom (TT) koji se protezao u donju šuplju venu (DŠV). Prikazani bolesnici su lečeni u našoj ustanovi između januara 1995. i oktobra 2021. godine. **Rezultati**. U navedenom periodu operisana su 92 bolesnika (72 muškarca i 20 žena), prosečne starosti od 60,5 godina. Kod 73,33% bolesnika postojala je predominacija desnostranog tumora. Bolesnici sa TT u bubrežnoj veni (nivoa 0 i I) nisu bili uključeni. Nivoi TT II, III i IV bili su prisutni kod 32 (34,8%), 52 (56,5%) i 8 (8,7%) bolesnika, redom. Jedan bolesnik imao je tromb u desnoj plućnoj arteriji. Četiri bolesnika imala su metastaze u jetri, a kod deset bolesnika bili su zahvaćeni limfni čvorovi. Hirurški pristup subkostalnom incizijom bio je postignut kod 8 (8,69%) bolesnika, *chevron* rezom kod 11 (11,95%) bolesnika, dok je kod 73 (79,34%) bolesnika bila urađena sternotomija i subkostalna/*chevron* incizija. Intraoperativno, postojala je jedna komplikacija u vidu plućne

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tromboembolije. Kod šest bolesnika bilo je potrebno izvršiti reoperaciju zbog krvarenja iz operativne rane. Trogodišnje preživljavanje bolesnika sa tumorom bubrega i TT nivoa II−IV u DŠV iznosilo je 43%. **Zaključak.** Operacija će ostati primarni metod lečenja bolesnika sa tumorom bubrega i TT u DŠV. Dugotrajno preživljavanje tih bolesnika može se postići samo potpunim hirurškim uklanjanjem (radikalna nefrektomija i trombektomija).

**Ključne reči:**
**bubreg, neoplazme; neoplazme, metastaze; v. cava inferior; hirurgija, operativne procedure; preživljavanje.**

## Introduction

The most common type of kidney malignancy is renal cell carcinoma (RCC), and it is twice as common in men than in women. RCC ranks sixth among all malignancies in men and seventh in women [1]. This malignancy is associated with proliferation into the *inferior vena cava* (IVC) in 4–10% of cases, and in 1% of patients, the tumor thrombus (TT) spreads to the right atrium [2–4]. Patients with RCC and TT in the IVC treated with nephrectomy alone without thrombus evacuation have a poor prognosis and die within one year from diagnosis [5]. Modern surgery imposes multidisciplinary treatment of diseases that, until recently, were the subject of only certain specialties. In addition to the urologist who treats the underlying disease and performs nephrectomy, the operative team also consists of surgeons of other specialties, primarily vascular surgeons, as well as cardio and abdominal surgeons. The operation is performed in the cardiovascular room due to the possible cardiopulmonary bypass (CPB). The anesthesiologist must be familiar with cardiovascular and thoracic surgeries and use cardiovascular arrest, extracorporeal circulation (ECC), and venous bypass [6, 7].

The aim of this study was to present the results of radical nephrectomy and thrombectomy in patients with renal tumor and TT extending into the IVC performed in the last 25 years at our institution.

## Methods

From January 1995 to October 2021 at the Clinic of Urology and the Clinic for Vascular and Endovascular Surgery of the Military Medical Academy in Belgrade, Serbia, patients with RCC and TT in the IVC were treated with radical nephrectomy, including extraction of TT from the IVC. Although RCC can be present in a variety of clinical forms, from asymptomatic, accidental findings to metastatic manifestations, patients with TT most often have symptoms presented [2]. Local pain and hematuria may be the result of local tumor growth. Other symptoms include nausea, fatigue, and weight loss as a part of the paraneoplastic syndrome. Specific symptoms may appear due to the IVC occlusion, lower extremity edema, new varicocele, pulmonary thromboembolism (PTE), ascites, Budd-Chiari syndrome, *caput medusae*, cardiac dysfunction, and symptoms of metastatic disease [2, 6, 7]. Ultrasound is used for quick orientation along with the clinical picture and symptoms. With good visualization and dimensions of the tumor in the kidney, it is necessary to look for infiltration of adipose retroperitoneal tissue, lymphadenopathy, and intraabdominal metastases. Initial diagnosis includes multislice computed tomography (MSCT) and portocavography; however, magnetic resonance imaging (MRI) finding also reveals TT enlargement and degree of the IVC occlusion. Transthoracic echocardiography is used to confirm the presence of TT in the right atrium. Classification of TT levels is extremely important because it is the basis for surgery planning. Montie et al. [8] from the Mayo Clinic classify TT levels as shown in Table 1. We used that classification to estimate thrombus levels.

### *Surgical technique*

The aim of the surgical treatment of renal tumors involving TT in the IVC is to remove all tumor tissue. With nephrectomy of the affected kidney, it is necessary to perform the IVC thrombectomy or its resection with or without reconstruction, retroperitoneal lymphadenectomy, and metastasis removal. The patient lies on their back with arms outstretched under endotracheal anesthesia. The procedure begins with a medial sternotomy and the IVC control in the supradiaphragmatic, intrapericardial part just before the IVC enters the right atrium. The IVC clamping or tourniquet in this section prevents PTE during IVC surgery and manipulation. The incision on the anterior abdominal wall is usually subcostal or bi-subcostal (chevron) but can also be approached by medial laparotomy. The decision on the unilateral subcostal incision or chevron approach is made depending on the location (side) and size of the tumor. All patients with TT levels II and III are operated on through a

**Table 1**

**Classification of tumor thrombus (TT) levels in patients with renal tumor and TT in the *inferior vena cava* (IVC) [8]**

| TT level | Definition |
|---|---|
| 0 | Thrombus confined to the renal vein or on a pathological preparation. |
| I | Thrombus spreads in the IVC < 2 cm above the renal vein. |
| II | Thrombus spreads > 2 cm above the renal vein but below the hepatic veins. |
| III | Thrombus at or above the hepatic veins but below the diaphragm. |
| IV | Thrombus spreads above the diaphragm. |

unilateral (right kidney)/bilateral-chevron (left kidney) subcostal incision and sternotomy. First, the renal artery is ligated because it results in the mobilization of the kidney with the tumor, reduces bleeding, and often retracts TT [9]. The IVC thrombectomy depends on the TT level. All patients are treated with a low dose of heparin for five to seven days postoperatively.

*Tumor thrombus levels 0 and I*

TT levels 0 and I enter the IVC minimally and do not obstruct it, so there is no need for sternotomy and PTE protection. These levels were excluded from this study because a vascular and/or cardiac surgeon was not involved in operation procedures in these cases. Accordingly, this analysis was focused on higher levels of malignant TT propagation.

*Tumor thrombus levels II and III*

TT level II requires more extensive IVC dissection to achieve thrombus themes. The upper border of the thrombus is usually determined by gentle palpation, less often with ultrasound. Unequivocally, it is necessary to put vascular loops on the subhepatic IVC, infrarenal IVC, and both renal veins to secure the patient from massive vein bleeding. This technique provides complete vascular control but does not prevent PTE if used without protection. Sometimes, it is necessary to ligate accessory hepatic veins from the caudate lobe to make a place for the subhepatic clamp. Pringle's maneuver interrupts blood flow to the liver through the portal vein and hepatic artery, thus reducing bleeding from hepatic veins after thrombus extraction and preventing liver congestion during the IVC clamping [10]. At TT levels II and III, an L-shaped IVC incision is made from the renal vein confluence over the IVC to the proximal [9]. TT is gently separated with fingers or a vascular instrument with a dissector (probe), and the renal vein ostium is cut off and can often be removed as a single specimen. Due to the fragile consistency of TT, it often disintegrates and removes several parts. The IVC lumen is washed with saline, and any remaining thrombus is inspected and subsequently extirpated. Part of the IVC wall around the ostium is biopsied and sent for histological verification. TT is often extirpated completely because a smaller thrombus does not adhere to the IVC wall; however, a larger thrombus that completely obstructs the IVC and reaches the hepatic veins adheres, leaving a thin layer fixed to the IVC wall. In that case, resection of the IVC with reconstruction should be considered. After thrombectomy, the tourniquet on the hepatoduodenal ligament (Pringle) is loosened to flush out any remaining thrombus and air, and the vascular clamp is placed infrahepatically. The hole on the IVC is sewn with polypropylene suture (Prolen® 4–0). The last suture is left untouched so that after releasing the remaining clamps, the bloodstream can expel any blood clots and air, after which it is tightened [11, 12]. At the moment of releasing the clamp, an anesthesiologist helps by increasing the pressure in the pulmonary bloodstream to ensure a constant venous inflow and ventilation of the IVC. If a blood thrombus is present along with the tumor, the patient is prescribed anticoagulant therapy in order to prevent venous thrombosis and the focus of thromboembolism.

*Tumor thrombus level IV*

TT level IV is the most complicated part of the surgical treatment of TT in the IVC. The safest and most common way to extirpate a tumor from the right atrium would be through a sternotomy, with CPB and arrest. After establishing the ECC, a longitudinal incision about 3 cm long is made on the front of the right atrium. If the thrombus is larger, then extraction is performed, and if it is smaller and not fixed, it is possible to manually push it back into the IVC and place a vascular clamp or tourniquet above it. In the second act of the operation, the thrombus is removed, as in the case of TT level III, through an abdominal incision. This maneuver is useful in compact tumors that have not adhered to the atrial wall and when the incision is performed on a beating heart without CPB. After extraction or distal repositioning, the incision is closed with Prolen® 4–0 suture. The clamp or tourniquet on the IVC near the atrium wall must stand until the end of the operation so that we do not artificially provoke PTE.

*Anesthesiological technique*

All patients underwent surgery under balanced general endotracheal anesthesia. After standard premedication, intravenous anesthesia (benzodiazepines, opioids, intravenous anesthetic, and muscle relaxant) is administered. An inhalation anesthetic (sevoflurane) is used as a standard to maintain anesthesia with the additional use of opioids and muscle relaxants. In most patients, unless there are contraindications or technical limitations, an epidural catheter is used for intraoperative and postoperative analgesia. For patients with levels II, III, and IV thrombus propagations into the IVC, epidural morphine in a dose of 2–4 mg is used with local anesthetics. In addition to standard monitoring, invasive monitoring is applied (arterial line for invasive continuous measurement of arterial pressure, central venous catheter for monitoring central venous pressure). All patients undergo a nasogastric tube at the introduction. Patients are heated during surgery using external heaters and heated intravenous fluid infusions. Vasopressors (noradrenaline or phenylephrine) are used to maintain perfusion pressure during the critical phases of the operation (clamping or placing the ligature on the IVC at different heights). Activating clotting time monitoring is used intraoperatively to monitor anticoagulation (heparin) in patients with TT level IV. At other levels, intraoperative use of heparin is not used. According to the indication, viscoelastic tests (Rotational Thromboelastometry – ROTEM) with targeted correction of hemostasis disorders are used in the patients. All patients are scheduled for extubation within 6–8 hrs after completing the intervention.

**Results**

In our series, we operated on 92 patients (72 men and 20 women) with renal tumors that invaded the IVC, with an average age of 60.5 years (32 to 81 years). There was a right-sided dominance of the tumor in 73.33% of patients. TT levels II, III, and IV were present in 32 (34.8%), 52 (56.5%), and 8 (8.7%) patients, respectively. Localization of renal tumor and TT level, confirmed by MSCT, is shown in Figure 1.

The operative approach involved a subcostal incision in 8 (8.69%) patients and a chevron (bilateral subcostal incision) in 11 (11.95%) patients. In the remaining 73 (79.34%) patients, the surgical approach was subcostal (right kidney) /chevron (left kidney) with sternotomy due to PTE protection (Figure 2).

In one case, we performed the IVC restraint through an anterior right thoracotomy because the patient had previously had a sternotomy with aortocoronary bypass surgery. All patients underwent radical nephrectomy with the extraction of the TT from the IVC (Figure 3).

In 92.3% of patients, RCC was histopathologically confirmed, while lymphoma, Ewing sarcoma, and transitional cell carcinoma were present in 2.2% of patients and adult Wilms tumor in 1.1% of patients. Preoperatively, 87% of patients had significant comorbidity, of which 52.1% had cardiac disease, while 19.6% had diabetes mellitus.

CPB was used four times in patients with TT level IV, where TT filled the entire atrium, and all passed without complications (Figure 4).

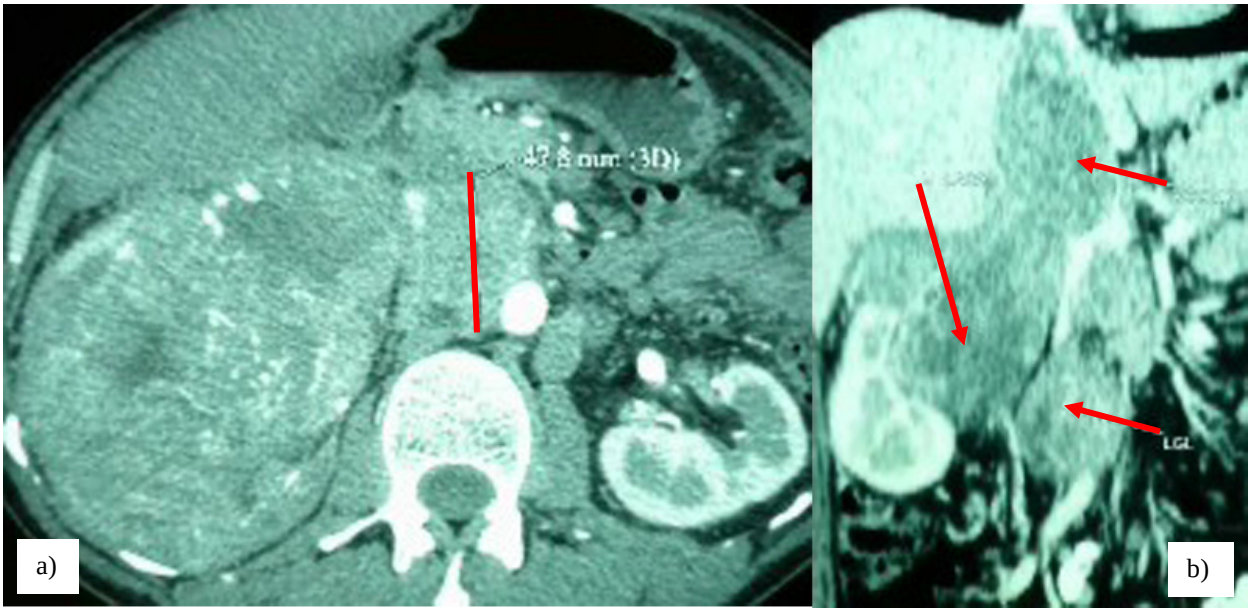


**Fig. 1 – Multi-slice computed tomography cavography. a) The *inferior vena cava* (IVC), 47 mm in diameter, filled completely with tumor thrombus (TT); b) Diaphragm level (TT level III): tumor (upper left arrow), IVC with TT (upper right arrow), lymph node (lower right arrow).**


**Fig. 2 – a) Sternotomy and chevron for left-sided tumor and tumor thrombus (TT) level III; b) Loop on the *inferior vena cava* beneath the right atrium; c) Sternotomy and right subcostal incision for right-sided tumor and TT level III.**

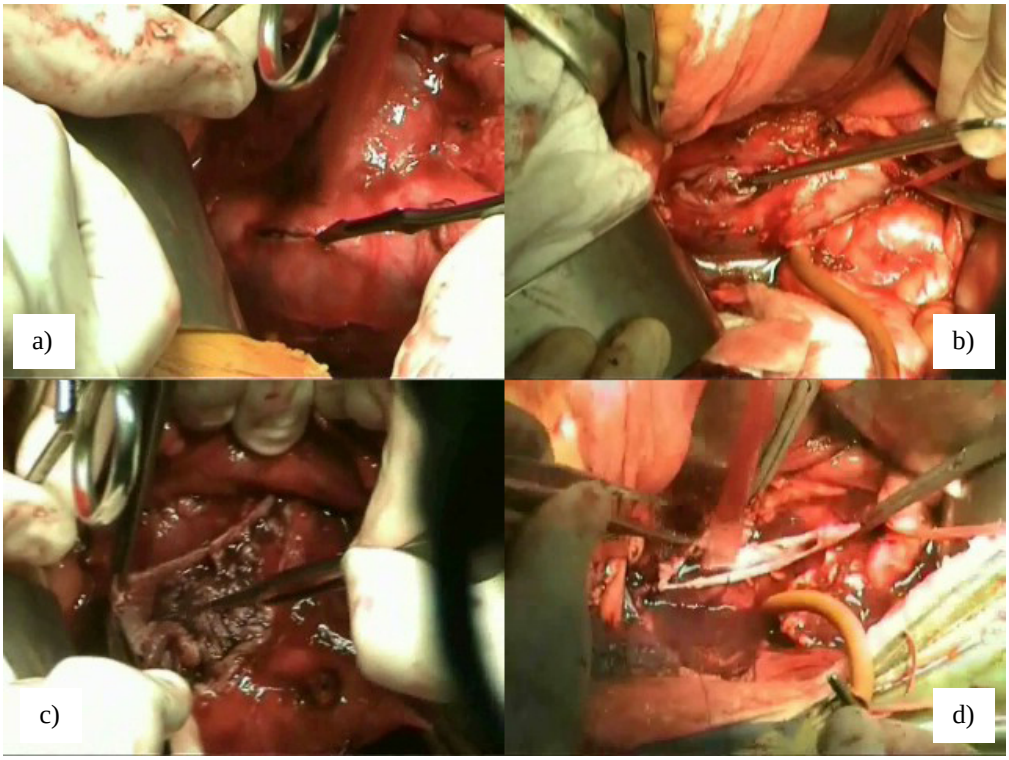


**Fig. 3 – a) The *inferior vena cava* (IVC) anterior incision; b) Completed IVC incision; c) Thrombus extirpation; d) Sewing the hole on the IVC.**

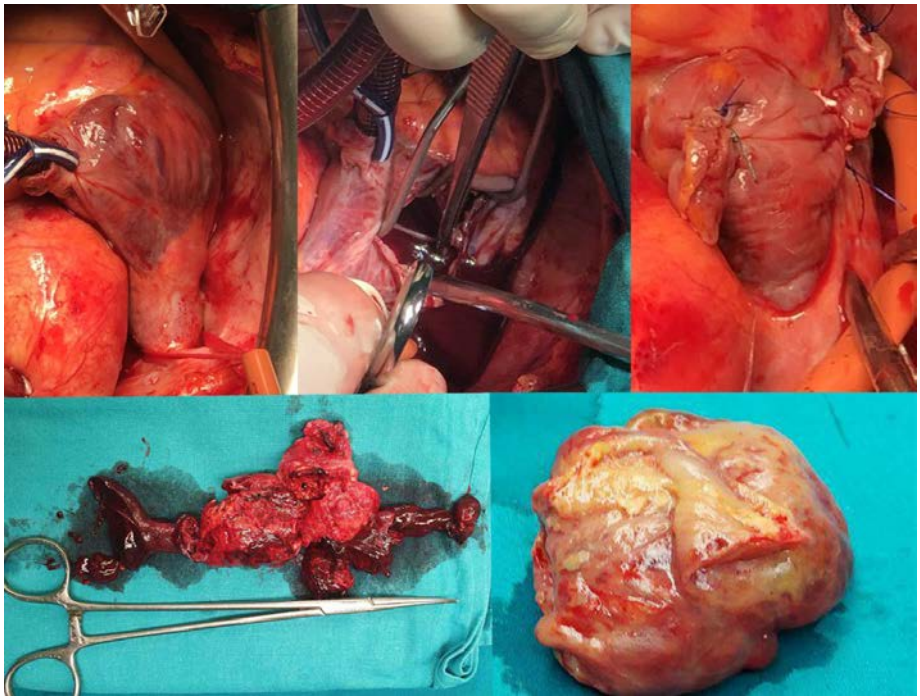

**Fig. 4 − Extirpation of tumor thrombus from the right atrium (upper parts of the display), extirpated thrombus in its entirety (lower parts of the display). Extracorporeal circulation was applied.**

With the "beating heart" technique, we operated on three patients without complications; one case was operated on an intermittent cardiac arrest.

The average duration of the operation was 180 min. Intraoperative and early postoperative blood loss initially ranged from 500 to 15,000 mL; the average dose of blood replacement was four units (1−26 units). In the last five years, due to the developed technique, the bleeding during operation has been minimal and controlled, and it does not exceed 1,000 mL of blood with four units of compensation. No balloon occlusion with transesophageal echocardiography was used. There was no perioperative

mortality. The average number of hospital days was 14. The follow-up period covered, in the best case, 36 months from the operation due to the breakdown of a patient. In nine (9.78%) cases, an invasion of the excised IVC wall was noted (Figure 5).

Ten patients had tumor-altered lymph nodes in the interaortocaval and retrocaval positions. Four patients had solitary metastases in the liver, and one patient had, in addition to the TT level III, an echinococcal cyst that was extirpated in the same act. Six (6.52%) patients required re-exploration after surgery due to bleeding. All bleeding was diffuse in nature when hemostasis was established by the replacement of blood elements and plasma. Six splenectomies were reported. There were four cases of subsequent blood thrombosis of the IVC without clinical significance. We had one iatrogenic intraoperative PTE when we did not use protection during sternotomy. By prompt reaction, we extracted a thrombus from the pulmonary artery, and the patient (34 years old) survived the operation without consequences. Late complications from 30 days to one year after the surgery included chronic kidney insufficiency in about a third of operated patients and recurrences of the underlying disease. Eight recurrences of TT in the IVC were reported (two TT level IV, five TT level III, and one TT at the incision site). TT levels III and IV recurrences due to advanced disease were not reoperated. A patient who developed a recurrence at the IVC incision site after three months was reoperated. The reoperation revealed the entry of TT through the lumbar vein, which was free in the primary operation. The patient was alive 13 years after reoperation without signs of recurrence [13]. Estimation of survival was difficult because about 25% of the patients did not report for check-ups at our institution due to the distance from our Center and the COVID-19 pandemic in the last two years. According to the available result findings, due to renal tumor with TT in the renal vein and/or IVC, the total three-year survival rate in our series of all patients operated on was 81%, which is not significantly different from the survival of renal tumor patients without TT invading the IVC. For the isolated group of patients with TT levels II–IV, for which data were available, the three-year survival rate was 43%. In 10% of these patients, the fatal outcome was due to diseases unrelated to the kidney tumor.

## Discussion

In 4–10% of cases, untreated kidney tumors get complicated by the formation of TT in the renal vein that spreads to the right atrium in 1% of patients and PTE with a poor outcome. The median survival time of the non-operated patients is five months, and the one-year survival rate is 29% [14]. Significantly better survival is achieved by evacuating the TT from the IVC with nephrectomy, especially in the absence of distant metastases and regional

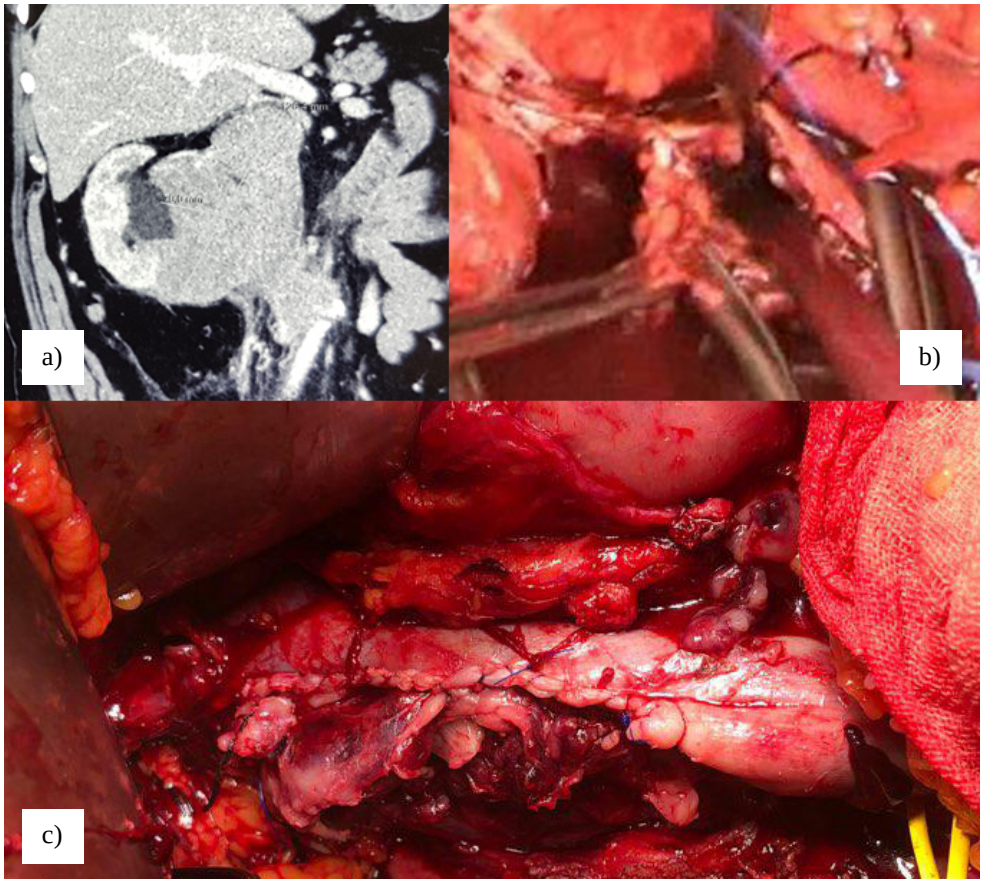


**Fig. 5 – a) Multi-slice computed tomography of the right kidney and tumor thrombus (TT); b) Extraction of TT and biopsy of *inferior vena cava* (IVC); c) Sewed IVC with clear signs of tumor infiltration.**

lymph node involvement. With this treatment of TT levels II–IV, three- and five-year survival rates are up to 39–43% and 58–60%, respectively [9, 15–17]. By combining the knowledge of several surgical specialties, far more significant and better results can be achieved in the group of patients who were, until recently, incurable [18]. For these reasons, radical nephrectomy with the IVC thrombectomy has become the gold standard in treating these patients, with a two-to-five years' survival rate of 32−64% [10, 18]. This operation presents a challenge for the surgeon due to potential massive bleeding and tumor thromboembolism [19]. Advanced intraoperative and postoperative anesthesia support allows far more aggressive surgical approaches and procedures [19, 20]. With the advancement of immunotherapy [21, 22], control of distant metastases can be achieved in patients with renal tumors spreading into the IVC so that their survival is prolonged if more aggressive surgical therapy is performed [23]. Retrohepatic and supradiaphragmatic localization of TT is a real challenge for the surgeon. The proximity and possible involvement of the hepatic veins, the proximity of the right atrium, and the poor exposure of the retrohepatic part of the IVC are the facts that make this procedure extremely difficult to perform. One technique cannot be applied to all patients, and a surgical plan is made for each patient individually. The optimal procedure is planned based on preoperative diagnostics, especially according to the level of occlusion and the added blood clot distally. Typically, the TT level IV involves CPB and circulatory arrest so that the tumor can be easily extirpated from the atrium [7]. However, if surgery is continued under the CPB, increased bleeding may occur due to nephrectomy because the patient is completely heparinized. That prolongs the time of surgery and anesthesia and increases the risk of postoperative coagulopathy. In our patients, after extirpation of TT from the atrium, we discontinued CPB and reversed the effect of heparin with an adequate dose of protamine. Renal artery embolization can be performed preoperatively to reduce blood loss and achieve the reduction of tumor and TT partially, transferring it to a lower stage [24]. We used this procedure four times at the beginning of the series, but we significantly reduced the bleeding by improving the surgical technique. Prevention of PTE can be achieved by placing an endoluminal balloon catheter [25]. However, there is a great risk of the IVC wall bursting, and passing a catheter through TT can lead to embolization. Furthermore, some authors suggested a transabdominal approach to avoid CPB and sternotomy by liver mobilization and transdiaphragmal path to the pericard and the IVC control [26–28]. In our series, prevention of distal embolization was achieved by placing a tourniquet on the IVC just below the right atrium through a sternotomy. Isolated sternotomy, as protection against PTE, is proven to be an extremely safe and effective procedure. Suspected invasion of the IVC wall probably requires partial or total resection with the IVC vascular reconstruction to maximize cancer control [29, 30]. In our patients, we did not resect the IVC, so there was no need for placing a graft. Alternatively, fully occluded IVC can be safely ligated, or IVC resection (cavectomy) can be performed without significant morbidity [30], but we did not use that method in our series. Postoperatively, in patients with IVC TT, low-dose heparin therapy was prescribed for a period of five to seven days. About 15% of patients have early complications up to 30 days after the operation. Perioperative mortality involves about 2–3% of patients [1], and up to 7.5% occur due to hemorrhagic complications [3]. The need for transfusion during and immediately after the surgery increases with TT levels. Early complications are associated with TT levels. As many as 46.9% of patients with TT level IV have early complications compared to level 0, where 12.4% of patients experience early complications. Splenectomy and IVC thrombosis are not rare [25]. Although some authors show that the ten-year survival rate is significantly lower if the thrombus is above the diaphragm [3], there is no significant difference in the patient's outcome depending on the TT level [7]. Nonmetastatic renal tumor with spread into the IVC is potentially curable if complete tumor removal is performed [31].

## Conclusion

The treatment outcome has been improved, thus reducing morbidity and mortality. The progress in reducing morbidity and mortality and in improving the treatment outcome of patients with renal tumors and TT invading the IVC is provided by an aggressive surgical procedure. This procedure can also be used if there are resectable distant metastases; it can also be performed as a palliative procedure. Preoperative determination of TT levels is crucial in planning surgery for kidney tumors with thrombus in the IVC. Sternotomy used in our patients did not increase intraoperative mortality and morbidity compared to the other studies in which only the transabdominal approach was used. PTE with TT is the most severe perioperative complication, with a mortality rate of up to 75%. The use of IVC control through sternotomy eliminates the risk of intraoperative PTE.

Surgery will remain the primary method of treatment in cases where renal tumors involve the IVC with TT. Long-term survival in these patients can only be achieved by complete surgical removal (radical nephrectomy and thrombectomy). Until now, these patients have been considered inoperable with a fatal outcome within one year, so this procedure significantly improves the results of their treatment outcome.

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