

Vein-associated tumors: Our six-year surgical experiences in Başkent University Ankara Hospital

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ABSTRACT

Objectives: In this study, we present our surgical management strategy in inferior vena cava (IVC) vein-associated tumors and discuss clinical results.

Patients and methods: Between January 2014 and December 2020, a total of 16 vein-associated tumor cases (10 males, 6 females; median age: 56.3 years; range, 39 to 69 years) operated in our clinic were retrospectively analyzed. These tumors included 10 renal cell carcinomas (RCCs), two IVC leiomyomas, one IVC leiomyosarcoma, one right subclavian vein-associated lipoma, and one tumor with IVC compression due to right renal artery aneurysm.

Results: Ten of the patients were RCCs, of three were leiomyomas, of one was leiomyosarcoma, and of one was lipoma. The RCC constituted the majority of vein-associated tumors. The IVC involvement was present in all patients. Extracorporeal circulation was required in three (30%) of the RCC patients during the operation. During postoperative follow-up, venous thromboembolism development was observed in five patients, and two patients had IVC total thrombosis.

Conclusion: A multidisciplinary approach, such as the approach to RCC, can be applied in the management of large vein-associated tumors with low complication and mortality rates, particularly in benign lesions.

Keywords: Carcinoma, leiomyoma, leiomyosarcoma, renal cell.

Tumors associated with the inferior vena cava (IVC) and iliac veins are mostly malignant.^[1-5] Leiomyosarcoma is the most common of the primary tumors,^[2,3,5-10] while secondary tumors are often of genitourinary, colorectal, and hepatic origin.^[2-4] Leiomyosarcoma most commonly occurs at the suprarenal segment of IVC.^[2,3,11] Secondary tumors are more common, and the most common of these is renal cell carcinoma (RCC). This type of carcinoma has a specific feature due to the tumor invasion into the IVC lumen. The tumor may extend to any segment between the renal-caval junction

and the right atrium. This specific feature is seen in approximately 10% of patients and, furthermore, this ratio is related to the tumor size.^[8-10] In addition, adrenocortical tumors and sometimes gynecological malignancies can also cause tumor thrombi extending into the iliac vein and IVC.^[2,3,12] Other vein-associated secondary malignancies are local spread of urogynecological tumors and lymph node metastases. These can cause external compression, vessel wall invasion, and intraluminal tumor thrombi.^[1,12,13] The most common types of these secondary tumors are RCC, urothelial carcinomas, adrenal tumors, Wilms

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tumor, leiomyoma, leiomyosarcoma, lipoma, and hepatocellular carcinomas.^[13,14]

The common feature of almost all of these vein-associated tumors is that the survey is very short without surgical treatment.^[15,16] While surgical management of tumors associated with the iliac vein and infrarenal vena cava level is optimal, surgery is more challenging for tumors associated with IVC at the suprarenal level. The reasons for this difficulty include more complex vascular structures at the suprarenal level, the liver complicating the surgical exposure, and the lack of clamping space for vascular repair or transposition.^[5] Since RCC is the most common tumor causing tumor thrombus, this type of cancer has been the main focus of studies. Several classifications have been made for management of the vein-associated tumors regarding the extent of the tumor.^[17-19] Novick classification is one of them and this classification is also used in our clinic.^[18]

The main goal of treatment is to achieve complete revascularization with complete surgical resection. While this can be achieved with graft interposition after simple clamping in low-stage tumors, it can only be achieved with extracorporeal circulation support and even total circulatory arrest in higher-stage tumors. It is possible to manage this management with a multidisciplinary preoperative evaluation, which mostly includes an experienced cardiovascular surgeon, urologist, general surgeon, obstetric surgeon, cardiologist, radiologist and anesthesiologist.

In the present study, we aimed to present our surgical management strategy in vein-associated tumors and discuss the clinical results.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Başkent University Hospital, Ankara, Türkiye, Department of Cardiovascular Surgery, between January 2014 and December 2020. A total of 16 vein-associated tumor cases (10 males, 6 females; median age: 56.3 years; range, 39 to 69 years) operated in our clinic were included. Data were retrospectively reviewed from the patients' clinic and outpatient clinic files. The tumors included 10 RCCs, three IVC leiomyomas, one IVC leiomyosarcoma, one right subclavian vein-associated lipoma, and one tumor with IVC compression due to right renal artery aneurysm. Data including age, sex, tumor type, tumor location, diagnostic methods and procedures were recorded. Patients over 18 years of age who had a vein associated

tumor were included. Preoperative evaluation was carried out with a task, which included gynecology, urology, cardiovascular surgery, general surgery and anesthesia teams according to the tumor type. Only artery-associated tumors and other tumors that did not undergo vascular repair, but were included in the operation were excluded.

Operation procedure

Preoperative classification and reconstruction: Preoperative classification was performed according to the Novick in patients with IVC infiltrating tumors diagnosed with RCC.^[18] During the operation, primarily the venous system was attempted to be protected with primary repair. Cases were managed with tumor excision and repair of the vascular structure, primarily by preserving the vein, and if this could not be achieved, tumor excision and grafting approach were used. Primary closure was performed to allow up to 50% stenosis in the IVC, and if venoplasty was to be performed, repair was performed with a vascular patch. Vascular patch was also used for the repair of the iliac veins. Iliac ligation and graft interposition were not performed. While primary closure was used as the primary option in simultaneous arterial interventions, a polytetrafluoroethylene (PTFE) vascular prosthesis graft was used in cases requiring graft interposition. In one patient who had renal artery aneurysm, the kidney resected after IVC graft interposition was auto-transplanted into the right iliac vein. Total circulatory arrest was performed in the same patient due to tumor-like invasion and adhesion to the renal vein. Also, cardiopulmonary bypass (CPB) was performed in a total of four patients. Two of these were type 3 RCC and the other two were leiomyoma at the hepatic vein level of the IVC.

Postoperative follow-up: The patients who were followed under low-molecular-weight heparin (LMWH) treatment during hospitalization were also followed with anticoagulant treatment in the postoperative period. The patients with suspicious symptoms related to vascular patency were first examined with ultrasonography, and if an abnormality was detected in this examination, advanced imaging methods were performed with computed tomography (CT) angiography or magnetic resonance angiography (MRA).

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Mac Version 20.0 software (IBM Corp. Armonk, NY, USA). Continuous variables were

Table 1. Baseline data of the patients and procedural data (n=16)

	n	%	Mean±SD	Median	Min-Max
Mean age (year)				56.3	39-69
Sex					
Male	10	62.5			
Tumor					
RCC	10	62.5			
Non-RCC	6	37.5			
Distant metastasis	6	37.5			
Vein					
IVC	13	81.25			
IVC+RIV	1	6.25			
RIV	1	6.25			
RSCV	1	6.25			
Reconstruction					
Primer	15	93.75			
Patch	1	6.25			
Cardiopulmonary bypass	6	37.5			
Complication	4	25			
Hospital stay (days)			10.8±9.8		
IVC filter	5	31.25			
Venous thromboembolism	5	31.25			
Anticoagulation					
LMWH	15	93.75			
DOAC	1	6.25			
Follow-up (month)			28.6±28.7		
Mortality	6	37.5			

SD: Standard deviation; RCC: Renal cell carcinoma; IVC: Inferior vena cava; RIV: Right iliac vein; RSCV: Right subclavian vein; LMWH: Low molecular weight heparin; DOAC: Direct oral anticoagulants.

expressed in median (min-max), while categorical variables were expressed in number and frequency. The Student t-test was used for the normally distributed data measured on a continuous/interval scale, while the Mann-Whitney U test was used for the non-normally distributed data. Cox regression (or proportional hazards regression) analysis was used as a method for investigating the effect of variables on the time a specified event takes to happen.

RESULTS

Baseline data of the patients are summarized in Table 1. Ten of the patients were RCC, of three were leiomyomas, of one was leiomyosarcoma, and of one was lipoma. In addition, one case of renal artery aneurysm was included in this study due to its close relationship with the renal vein and IVC, and tumor-like behavior such as compression and adhesion. The RCC constituted the majority of vein-associated tumors. The IVC involvement was present in all patients. In the majority of the patients, it was

possible to repair peripherally, whereas in one patient due to IVC excision, a stenosis of more than 50% was repaired using a Dacron patch. Extracorporeal circulation was required in three of the RCC (30%) patients during the operation.

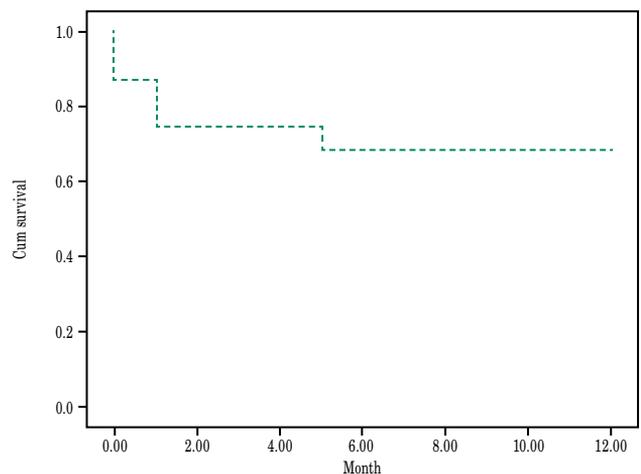


Figure 1. Kaplan Meier curve showing 12-month survival.

Table 2. Patients' data

No	Sex	Age	Tumor	Reconstruction	Vein	Follow-up	VTE	CPB	Complication	Mortality
1	Male	60	RCC	Primer	IVC	12	No	No	Diaphragmatic laceration	No
2	Male	68	RCC	Primer	IVC	35	No	No	No	No
3	Male	63	RCC	Primer	IVC	5	IVC total	No	Abdominal seroma	Yes
4	Male	43	RCC	Primer	IVC	1	IVC total	No	No	Yes
5	Female	57	RCC	Primer	IVC	0	No	Yes	No	Yes
6	Male	62	RCC	Patch	IVC	1	IVC partial	Yes	Splenic laceration	Yes
7	Male	69	RCC	Primer	IVC	71	No	No	No	No
8	Male	74	RCC	Primer	IVC	72	No	No	No	No
9	Male	41	RCC	Primer	IVC	18	IVC partial	No	No	Yes
10	Male	45	RCC	Primer	IVC	21	No	Yes	No	No
11	Female	69	Lipoma	Primer	Right subclavian	43	No	No	No	No
12	Female	39	Leiomyom	Primer	IVC+right iliac	29	Right iliac	Yes	No	No
13	Male	66	Renal artery aneurysm	Primer	RSCV	0	No	Yes	No	Yes
14	Female	56	Leiomyosarcom	Primer	Right iliac	14	No	No	Retroperitoneal abscess	No
15	Female	40	Leiomyom	Primer	IVC	72	No	No	No	No
16	Female	50	Leiomyom	Primer	RIV	72	No	Yes	No	No

RCC: Renal cell carcinoma; VTE: Venous thromboembolism; CPB: Cardiopulmonary bypass; IVC: Inferior vena cava; RIV: Right iliac vein; RSCV: Right subclavian vein.

Major involvement was IVC due to RCC invasion. In addition, one patient had a compression effect due to a right subclavian lipoma. In RCC patients, after radical nephrectomy, angioplasty was performed vascular patch in one patient and primary repair was performed in other patients.

In the postoperative follow-up, venous thromboembolism (VTE) development was observed in five patients, and two patients had IVC total thrombosis. Auto-transplantation was performed in one patient after primary repair with CPB due to right renal vein and IVC injury. The CPB was required in a total of six patients. The IVC filter was needed in five patients. A total of six patients died during follow-up. In all patients, survival rate was 69% at 12 months (Figure 1). Also, patients' individual features are summarized in Table 2.

DISCUSSION

The major disease that determines our knowledge and management strategies in large vein-associated tumors is RCC. This is due to the fact that up to 10% of RCCs have a tumor thrombus, possibly extending from the renal vein to the right atrium. This route of spread of the tumor is well defined and several leveling systems exist. The reason for this leveling is mainly based on establishing certain standardization in the operations approach.

The experience gained by RCC may have provided similar management in rarer tumors such as intravenous leiomyoma and leiomyosarcoma.

Leiomyomatosis is a disease defined more than a century ago and can be classified as rare in non-uterine vascular structures.^[1,2,4] All patients with this disease, in which female sex is frequently affected, were also female in our study. Involvement of the disease can extend from uterine vascular structures to iliac veins, IVC and even intracardiac right structures. Accordingly, symptomatology may present with a wide spectrum, from leg swelling due to venous stasis to shortness of breath due to right heart failure. One of our patients had total thrombosis due to right common iliac vein involvement and this patient presented with massive leg swelling, while the other three patients had extremity edema findings due to IVC partial thrombosis. Leiomyomatosis that develops is thought to be a possible vascular involvement and a possible spread of uterine leiomyomatosis to the iliac vein or IVC. It is divided into four main stages according to the segment of spread iliac vein, IVC, and cardiac involvement. In one of our patients, left iliac vein reconstruction was performed after Stage 2 hysterectomy + bilateral oophorectomy. In this patient, cardiovascular surgery and gynecological surgery clinics worked together and no problem developed during the follow-up period of more than five years.

It is difficult to separate RCC from non-RCC tumors in cases with involvement of the great veins, particularly when they are at the level of the IVC. At this stage, the diagnosis of RCC tumors can be made accurately by CT and magnetic resonance imaging (MRI) in the preoperative period.^[20,21] Thus, it can be differentiated from other non-RCC tumors. We also use this imaging method in the preoperative differential diagnosis. Previously, the sex of the case was also a determining factor. While RCC comes to mind more in male patients with IVC-involved masses, non-RCC tumors are more frequently encountered in the female patient group.^[2,3] In our patient group, it is consistent with this finding with a sex ratio of 9:1 in the RCC patient group.

Surgically, it is possible for this classification to include the RCC classification. Stage 3 division of the Novick classification indicates tumor involvement between the IVC and the right atrium at the level of the renal vein. In this involvement, when the classification of RCC surgical approach is entered, even surgical management with CPB is required in patients with Novick 3 and 4 involvement. In a patient with Novick 3, primary IVC repair was performed with CPB, and right iliac vein thrombosis developed in the three-year follow-up of this patient and was treated with LMWH.

In the current study, when the RCC and non-RCC groups were evaluated proportionally, postoperative VTE (40% and 16.6%, respectively), in terms of complications (40% and 16.6%, respectively), CPB requirement (30% and 50%, respectively) and mortality (50% and 16.6%, respectively) were determined. Considering these data, the fact that RCC is malignant and prone to metastasis may explain the higher rates of VTE, complications, and mortality compared to the non-RCC group. On the other hand, although the use of CPB was higher in the non-RCC group, the lower complication and mortality rate may be related to the holistic surgery and multidisciplinary approach.

Although the survival rate was 73% in RCC at regional stage during five-year follow-up,^[22] this rate was lower at 12 months in our follow-up. The possible reason for this may be related to the increased mortality rate of RCCs with venous thrombus involvement at the suprahepatic level. This rate is 21% at the suprahepatic level, while it increases up to 80% at the infrahepatic level.^[23] This may be the reason for the decreased rate in our study.

The limitations of our study are non-randomization, retrospective design, and small sample size.

In conclusion, a multidisciplinary approach, such as the approach to RCC, can be applied in the management of large vein-associated tumors with low complication and mortality rates, particularly in benign lesions.

Ethics Committee Approval: The study was approved by Ethical Committee of Başkent University Medical School. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conception and design, provision of study materials or patients, collection, analysis and/or interpretation of data: D.Ş.; Provision of study materials or patients, collection, analysis and/or interpretation of data, drafting of the article: D.S.B.; Provision of study materials or patients, statistical expertise, drafting of the article: B.G.; Provision of study materials or patients, administrative, technical, or logistic support content, drafting of the article: A.S.; Provision of study materials or patients, administrative, technical, or logistic support content, collection, analysis and/or interpretation of data: Y.C.A., A.A., H.A.; Conception and design, administrative, technical, or logistic support content, statistical expertise, drafting of the article, critical revision of the article for important intellectual: H.T.A.

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