

# Outcomes in Renal Cell Carcinoma with Inferior Vena Cava Thrombus Treated with Surgery

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**ABSTRACT:** Introduction. Renal cell carcinoma can invade through the renal vein into the inferior vena cava, and can extend intraluminally, with tumor-thrombus formation. Methods: Retrospective study from January 2003 to August 2016. Surgical outcomes were analyzed. Neves classification was used for patient categorization. Kaplan Meier and Log-Rank test were used for survival analysis. Results: A total of 134 patients were included, 69 males (51.4%) and 65 females (49%), M:F ratio 1.06:1. Tumor size, bleeding and surgical time were higher in level IV thrombi (mean 16.1cm, 3 064ml and 6.5hrs, respectively), compared to level I (8.5cm, 1033ml and 3.1hrs, respectively). A higher frequency of positive lymph nodes was observed in levels III and IV compared with levels I and II (49% vs. 17.7%,  $p=0.0001$ ). Distant metastases were observed in 36 pts. (27%). Overall surgical mortality was 4.5%. 5-year overall survival was 63%. We observed a 5-year survival in patients with level I-II 82% and level III and IV 46%. Conclusions: Our results suggest the benefit for the patient of an aggressive surgical approach with an acceptable mortality and 5-year survival rate. The results obtained justify an aggressive surgical approach to these tumors.

**KEYWORDS:** Renal cancer, Thrombus, Inferior vena cava, Surgery, Urology.

## Introduction

Renal cell carcinoma (RCC) can produce tumor thrombi in up to 15% of cases, which can spread through the renal vein to the inferior vena cava [1].

The Neves-Zincke classification is used to define the level of the thrombus [2].

Identifying the level of tumor thrombus is an important step in surgical planning, given it dictates the surgical approach [3].

The therapeutic goal for renal cancer and tumor thrombus is complete resection of the renal tumor and concomitant successful elimination of the tumor thrombus [4,5,6,7].

In Mexico, renal cancer represents the 13th cause of cancer care [8].

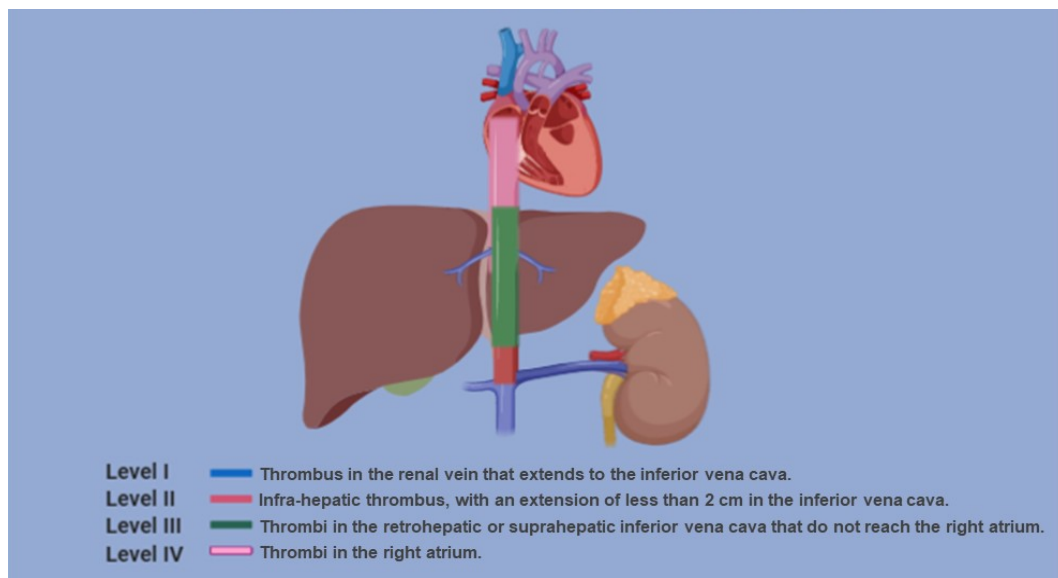
Many patients present at advanced stages, due to limited access to medical care, lack of awareness about health and socioeconomic status.

Our aim was to describe the outcomes observed in patients diagnosed with renal cancer and thrombus in the inferior vena cava treated with surgery at the Oncology Hospital, Centro Médico Nacional Siglo XXI, México City.

## Material and Methods

We conducted a descriptive, retrospective review of patients diagnosed with renal cancer who underwent nephrectomy and IVC thrombectomy at our Institution, the Oncology Hospital of the Centro Médico Nacional Siglo XXI, in Mexico City, from January 2003 to August 2016, according to the Neves classification (Figure 1).

After Institutional Board Review Approval of the protocol (R-2018-3602-027), each patient gave a written informed consent regarding their participation in the study.



**Figure 1. Renal cancer with thrombus in inferior vena cava, thrombus levels according to Neves classification.**

Standard preoperative protocols were carried out for all patients. Surgeries were performed jointly with cardiac and vascular surgeons in a cardiothoracic room.

All patients underwent surgery by midline abdominal incision and lumbotomy. Patients with involvement of the thrombus above the suprahepatic veins underwent thoracoabdominal approaches. For patients with involvement of the thrombus above the diaphragm, it was necessary to use cardiopulmonary bypass.

For the extraction of the thrombus, the surgical technique consisted of mobilization of the round ligament, the falciform ligament, the coronary and triangular ligaments, moving the liver towards the contralateral abdomen. All patients were followed at 60 months.

We analyzed surgical outcomes: complication major (hypovolemic shock, disseminated vascular coagulation, acute renal failure and septic shock); complication minor (metabolic ileus, atelectasis, metabolic acidosis, surgical wound hematoma and surgical wound infection); mortality; overall survival at 5 years.

We analyzed clinical characteristics: symptoms and signs, disease stage, surgical approach, operative findings, level of thrombus, postoperative complications.

Histopathological characteristics were obtained from pathology reports, analyzed in the pathology department of our hospital. The involvement of the vessel wall, perirenal fat invasion and N status was assessed by the histopathological report. To determine the histology, the Heidelberg classification of the World Health Organization (WHO) of 1997 was

used. The Fuhrman system was used in all histopathology assessment. Neves-Zincke classification was used for patient categorization.

### Statistical Analysis

For statistical analysis, we use Statistical Package for the Social Sciences (SPSS) version 23.0. The information was presented with 95% confidence intervals (CI).

We use the chi-square test to compare the categorical variables. We used the Kaplan-Meier test to estimate survival according to the level of the thrombus. We use log-rank to estimate the differences between the thrombus levels. For comparison purposes, we grouped patients into levels I-IV, in concordance to the TNM stage [9].

Stage pT3b is defined as the tumor thrombus below the diaphragm; while pT3c is defined as a thrombus located above the diaphragm. A value of  $p < 0.05$  was considered statistically significant.

### Results

142 patients were identified. Eight patients were excluded; 7 due to follow-up given at another institution, and 1 with an incomplete clinical record.

We describe the data of the remaining 134 patients, 69 males (51%), 65 females (49%). 64 years, was mean age (36-82 years).

Patients' characteristics according to the level of the thrombus are summarized on Table 1.

Table 1. Characteristics of patients.

Variables	Measurement scale	Level I 46 (%)	Level II 33 (%)	Level III 29(%)	Level IV 26(%)	p value
Gender	Male	25 (54)	19 (58)	15 (52)	10 (38)	0.49
	Female	21 (46)	14 (42)	14 (48)	16 (62)	
ECOG	0	17 (37)	10 (30)	5 (17)	5 (19)	0.55
	1	29 (63)	22 (67)	21 (73)	19 (73)	
	2	0 (0)	1 (3)	3 (10)	2 (8)	
Symptomatology	Incidentaloma	6 (13)	3 (9)	0	0	-----
	Triad (Hematuria, pain, tumor)	21 (45)	6 (18)	11 (38)	8 (31)	-----
Site	Right	29 (63)	21 (64)	20 (69)	20 (77)	0.63
	Left	17 (37)	12 (36)	9 (31)	6 (23)	
Approach	Lumbotomy	38 (83)	20 (61)	6 (21)	0	0.1
	Chevrón	8 (17)	12 (36)	14 (48)	3 (12)	
	Toracoabdominal	0	1 (3)	9 (31)	23 (88)	
Liver mobilization	Yes	0	6 (18)	18 (62)	24 (92)	0.1
Transoperative bleeding	Mililiters	1 033	1 487	1 510	3 064	-----
Surgery time	Hours	3.1	3.3	4.05	6.5	-----
Size of the tumor	Centimeters	8.5	10	13.4	16.1	-----
Positive lymph nodes	N0	40 (87)	25 (76)	15 (52)	13 (50)	0.001
	N1	6 (13)	8 (24)	14 (48)	13 (50)	
Metastases	M0	37 (80)	21 (64)	20 (69)	20 (77)	0.36
	M1	9 (20)	12 (36)	9 (31)	6 (23)	
Histology	Clear cells	39 (85)	27 (82)	23 (79)	22 (84)	0.99
	Papillary	3 (6)	2 (6)	2 (8)	2 (8)	
	Cromophobe	4 (9)	4 (12)	4 (13)	2 (8)	
Perirenal fat invasion	Yes	5 (11)	7 (21)	8 (26)	4 (15)	0.28
Furhman	I and II	23 (50)	11 (34)	10 (34)	10 (38)	0.40
	III and IV	23 (50)	22 (66)	19 (66)	16 (62)	
Trombus	Free	40 (87)	27 (82)	9 (31)	2 (8)	0.1
	Adhered to the vascular wall	5 (11)	6 (18)	16 (55)	17 (65)	
	Invades vascular wall	1 (2)	0	4 (14)	7 (27)	

ECOG: Eastern Cooperative Oncology Group

Mobilization of the liver, abdominal, and thoracoabdominal approaches was used more frequently in patients with thrombi at levels III and IV (89% and 76% respectively).

Only patients with thrombus in level IV merited cardiopulmonary bypass (CPB), 16 (61%) patients; with a median of 20.94 minutes.

Bleeding (3064ml, range 700-8000ml) and surgical time (6.5hrs, range 5-8.5hr) were higher, in level IV thrombi, compared to level I.

The tumor size was associated with Neves classification (mean tumor size 8.5cm level I vs. 16.1cm level IV).

In patients with thrombi levels III and IV, a greater number of patients with positive nodes was observed, when compared to levels I and II (49% versus 18%,  $p=0.0001$ ). 36 patients (27%) developed distant metastasis ( $p=0.36$ ).

We observed a 4.5% (6 patients) surgical mortality rate.

As major complication, we observed hypovolemic shock (4 pts.) disseminated vascular coagulation (4 pts.), acute renal failure (2 pts.) and septic shock (2 pts.) after the surgical event.

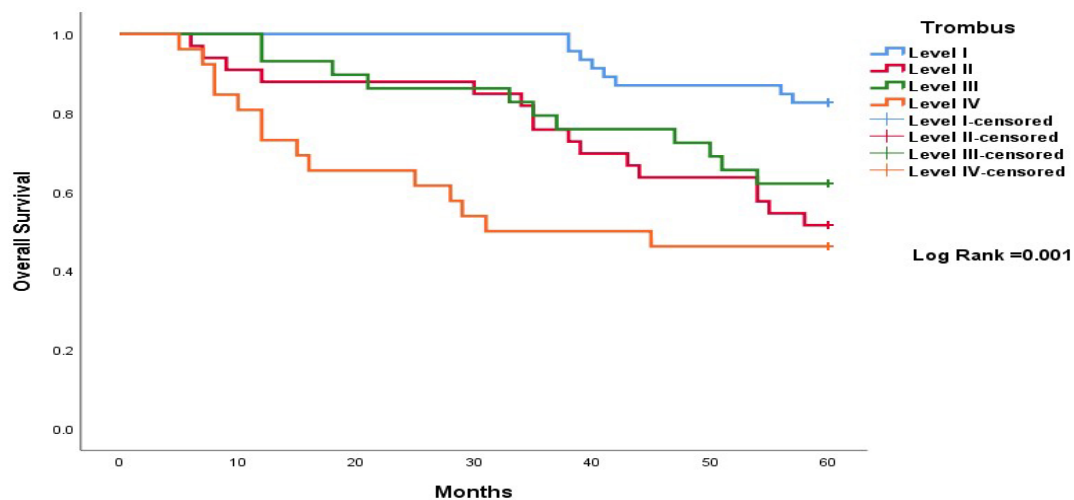
Minor complications 19% (25 patients), consisted of metabolic ileus, atelectasis, metabolic acidosis, surgical wound hematoma and surgical wound infection (Table 2).

Table 2. Major and minor surgical complications.

Variables	Measurement scale	Level I 46(%)	Level II 33(%)	Level III 29(%)	Level IV 26(%)
Complications	Major	1 (2)	3 (9)	4 (14)	4 (15)
	Minor	7 (15)	7 (21)	5 (17)	6 (23)

Median follow-up was of 60 months (48 range 72).

Five-year overall survival was higher in patients with level I-II thrombi versus level III-IV (82 vs. 46%) (Figure 2).



**Figure 2. Five-years overall survival in patients with renal cancer and inferior vena cava thrombus.**

## Discussion

In our cohort, we observed twice the frequency of level IV thrombi compared with previous reports. Probably due to the delay in seeking medical attention from our patients [10,11].

Also, this could be due to reference bias.

We observed a median age of 64 years, with an H: M 1.06: 1 ratio, similar to that reported by international studies, considering that the age of presentation of this cancer is these age groups [8,12,13].

In our study, we choose patients with Eastern Cooperative Oncology Group (ECOG) 0, I and II, patients with ECOG above II were not included, probably due to the comorbidities they must present, different from those reported by Haddad et al and Abel et al., the above as a variable that can modify our results [14,15].

We use the thoracic approach predominantly in thrombi located at level IV, due to the jointly intervention by the oncology urology team and the cardiothoracic surgery service. We use hepatic mobilization in levels II, III and IV, to have better vascular control, which allowed us to obtain a 30% lower bleeding in level III. Nevertheless, we got a 20% higher in level IV, than reported by Blute et al. Which could be due to the characteristics of tumors that undergo surgery in our service. When comparing the duration of the surgical procedure, we did not find differences with those reported by literature [16].

In our study, we observed a tumor size greater than reported by the literature, with median tumor of 12cm; and in levels III and IV, we observed a median tumor of 14.75cm,

approximately 50% higher than reported by Ciancio et al. and Haddad et al. Which probably contributes to the greater bleeding, but without increasing the duration of the procedure [13,14].

We observed 31% positive lymph nodes and 27% metastases, these findings may be related to the characteristics of the population, as well as the delay in requesting care by the patient, which affects tumors of greater volume and therefore with extension of the disease when compared with international studies [12,13,14].

In our study, we did not find, significant differences between postoperative complications and the level of location of the thrombus, similar to that reported by the literature [8,16]. We did not have deaths during the transoperative period, but we observed a postoperative mortality of 4.5%, which could be due to the characteristics of the selected patients, previously commented.

The limitations of our study are due to the retrospective nature, which includes the selection criteria, as well as the univariate analysis. Factors that may limit the results obtained.

When we compare our results with the literature, we observed higher survival rates at 5 years. Unlike Vázquez et al and Blute et al, in our study we found significant differences in 5-year survival according to thrombus level (log rank=0.001) [8,13,14,16].

Our data contrast in terms of overall 5-year survival, we consider it due to the high number of patients seen at our institution, our selection criteria, as well as to the expertise of the surgeons who perform this procedure, which could limit the reproducibility of the results.

## Conclusions

Our results suggest the benefit for the patient of an aggressive surgical approach with an acceptable mortality and 5-year survival rate.

The results obtained justify an aggressive surgical approach to these tumors.

## Conflict of interests

None to declare.

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