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RESEARCH

Postoperative mortality in renal cell carcinoma with vena cava thrombus in the elderly population (uroCCR study n°192)

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Abstract

Objective Inferior vena cava (IVC) thrombus is a severe presentation of renal cell carcinoma (RCC), traditionally treated by radical nephrectomy and thrombus extraction. However, the risk–benefit balance in elderly patients remains unclear due to limited data. This study aimed to assess surgical outcomes—particularly 90-day mortality—in patients aged ≥ 70 year and to identify risk factors for postoperative mortality.

Methods We retrospectively analyzed data from the prospective French UroCCR national cohort (2007–2023), including 298 patients with RCC with IVC thrombus who underwent surgery in 13 expert centers. Patients were stratified into ≥ 70 vs. < 70 year. The primary endpoint was 90-day mortality. Secondary outcomes included overall survival (OS), disease-specific survival (DSS), and predictors of 90-day postoperative mortality. Statistical analyses included univariate and multivariate logistic regression analyses adjusted for renal dysfunction.

Results Patients aged ≥ 70 year ($n = 117$) had a 90-day mortality rate of 10.5% compared with 5.5% in those < 70 year ($n = 181$; $p = 0.13$). Among patients aged ≥ 80 year ($n = 32$), the 90-day mortality increased to 19% ($p = 0.02$). Metastatic disease (OR 3.3, $p = 0.01$) and preoperative renal dysfunction (OR 3.9, $p = 0.02$) were significantly associated with 90-day mortality, with renal dysfunction remaining independently associated after adjustment for age (adjusted OR 2.8, $p = 0.04$). Long-term DSS did not differ between age groups. Study limitations include its retrospective design and the restriction of the cohort to surgical candidates treated in expert centers.

Conclusions Radical nephrectomy with thrombectomy provides acceptable outcomes in patients aged ≥ 70 year, although ≥ 80 year face higher perioperative risk. Careful patient selection, including thorough preoperative renal function assessment, is crucial. The comparable DSS suggests that age alone should not be considered a contraindication to surgery.

Keywords Elderly · Inferior vena cava thrombus · Nephrectomy · Perioperative mortality · Renal cell carcinoma · Surgical procedure

Introduction

An inferior vena cava (IVC) thrombus develops in 4–10% of patients with renal cell carcinoma (RCC) [1, 2] and is associated with an unfavorable prognosis [3]. Radical nephrectomy (RN) with cavotomy and thrombus extraction remains the only curative standard of care for non-metastatic patients with IVC thrombus [4]. Given the high risk of disease recurrence, adjuvant immunotherapy with pembrolizumab is now recommended [5]. For patients presenting with metastatic disease, systemic therapy is now preferred over surgery as the initial treatment, except in cases of severe symptoms. Surgery is considered in patients who demonstrate a favorable response to systemic therapy [4, 6].

The level of IVC involvement, as described in the Klein-Novick classification, serves as a key factor in disease management, although the association between thrombus level and oncological outcomes remains uncertain [2, 3]. Level III and IV thrombi may require complex surgical approaches, including thoracic intervention. The in-hospital

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mortality rate associated with this surgery is approximately 5% [7]. The five-year overall survival rate ranges from 40% to 50% but may be improved with immunotherapy. Deciding whether to proceed with surgery in elderly patients is challenging, especially in the context of advances in systemic therapies.

To date, only one study has specifically investigated perioperative morbidity and mortality associated with this procedure in elderly patients, analyzing a small cohort of 43 patients aged ≥ 70 year [8]. This study did not identify any significant differences in perioperative mortality, overall and disease-specific survival in this population, whereas larger series on renal cell carcinoma with IVC extension have identified age as a risk factor for in-hospital mortality [7].

The objective of this study was to compare surgical outcomes, particularly 90-day mortality, after RN with thrombus extraction in elderly patients, and to identify prognostic factors for postoperative mortality in this population.

Materials and methods

Study design, patient population and inclusion criteria

This study is based on data from the French national prospective renal cancer cohort (UroCCR). Eligible patients were retrospectively identified in the database between 2007 and 2023, and participating centers reviewed and validated the data for each case.

The database used the 2017 cTNM classification system for renal cell carcinoma. We included all patients with a confirmed diagnosis of renal cell carcinoma associated with an IVC thrombus confirmed on an abdominal CT scan or MRI, corresponding to cT3b and cT3c disease. Patients who did not undergo surgery and centers with fewer than four cases were excluded to reduce the number of centers and facilitate chart review.

Outcomes

The analysis compared patients aged ≥ 70 year (study group) with those aged < 70 year (control group). The primary prespecified outcome was 90-day mortality. Secondary outcomes included overall and specific-disease survival and predictive factors for perioperative mortality. We also planned an exploratory analysis for patients aged > 80 y. Additionally, we analyzed the clinical, biological, and radiological characteristics of the disease in both groups.

We used an eGFR threshold of 45 mL/min/1.73 m², calculated using the CKD-EPI formula, as a clinically meaningful cutoff for impaired renal function, because several studies have reported a marked increase in postoperative mortality below this threshold [9, 10].

Statistical analysis

Baseline characteristics were summarized using the median and interquartile range (IQR) for continuous variables, and percentages for categorical variables. Categorical variables were compared using Chi-squared or Fisher's exact test, as appropriate. Continuous variables were compared using Student's t-test or Mann–Whitney U test, depending on their distribution.

Logistic regression analyses were performed to identify predictors of 90-day postoperative mortality. A multivariable logistic regression model was performed, including variables with a p-value < 0.05 in the univariate analysis, within the limits imposed by the number of events.

Overall and disease-specific survival were estimated using the Kaplan–Meier method and compared using the log-rank test. Multivariable analyses were performed with Cox proportional hazards regression, adjusting for preoperative variables that differed significantly between groups and potential confounders, including sex distribution and ASA score.

All statistical analyses were two-sided, with a significance level set at 5%, and were performed using RStudio (version 4.4.2; R Foundation for Statistical Computing, Vienna, Austria).

Ethical considerations

This study was conducted in accordance with institutional and ethical guidelines as part of the UroCCR project (NCT03293563), which received Institutional Review Board (IRB) "Comité de Protection des Personnes Sud-Ouest et Outre-mer III" approval and authorization from the French Data Protection Authority (CNIL, number DR-2013-206). Decision no. DT-2024-027, dated December 31, 2024, authorized the Bordeaux University Hospital Center to implement automated data processing aimed at establishing a health data warehouse named "UroCCR" (authorization request no. 2231991).

All patients received oral and written information about the objectives and methodology of the UroCCR project and written informed consent was obtained.

Results

Table 1 Patient demographics and baseline characteristics

	All ($n=298$)	<70 y ($n=181$)	≥ 70 y ($n=117$)	p-value
Age at diagnostic - Median (IQR)	67 (68–74)	60 (54–66)	76 (72–80)	/
Sex category – n of male (%)	210 (70)	138 (76)	72 (62)	0.02
BMI - Median [IQR]	25 (23–29)	26 (19–26)	25.8 (20–28)	0.16
ASA score – n (%) 1 & 2 3 & 4	147 (55) 116 (44)	89 (61) 57 (39)	48 (45) 59 (55)	<0.01
ECOG – n (%) 0 & 1 2 & 3	229 (88) 32 (12)	143 (90) 16 (10)	86 (84) 16 (16)	0.54
Preoperative GFR (CKD-EPI) – n (%) >45 <45	239 (85) 43 (15)	154 (91) 16 (9)	86 (77) 26 (23)	<0.01
Hypertension – n (%)	156 (52)	82 (45)	74 (63)	<0.01
Anticoagulant – n (%)	65 (22)	28 (15)	37 (32)	0.01
Charlson Score – median [IQR]	4 (2–8)	3 (2–8)	5 (3–9)	<0.01
Tumor and extension – n (%)				
Symptoms at diagnostic – n (%)				
Local	138 (46)	88 (49)	50 (43)	0.44
Systemic	79 (27)	49 (27)	30 (26)	
Left side – n (%)	125 (42)	78 (43)	47 (40)	0.7
Size of tumor (cm) - median [IQR]	9 (7–11)	9.6 (7.2–12)	8 (6.1–10)	0.01
Level of thrombus (Klein Novick) – n (%)				
I & II	184 (62	106 (58)	78 (67)	0.2
III & IV	114 (38)	75 (41)	39 (34)	
Size of Thrombus (mm) - median [IQR]	44 (25–70)	42 (28–75)	44 (25–70)	0.16
cT stage – n (%)				
cT3b	258 (88)	155 (87)	103 (88)	0.2
cT3c	33 (11)	19 (11)	14 (12)	
cT4	4 (1)	4 (2)	0	
cN+ – n (%)	68 (23)	49 (27)	19 (17)	0.08
cM+ – n (%)	72 (24)	51 (28)	21 (18)	0.11
Histology – n (%)				
Clear cell	254 (85)	153 (84)	101 (85)	0.34
Papillary	23 (8)	11 (6)	12 (10)	
Others	23 (8)	17 (10)	6 (5)	
Surgery				
Robotic assistance – n (%)	30 (10)	15 (8)	15 (13)	0.28
Lymph node dissection – n (%)	136 (45)	88 (48)	48 (41)	0.24
Time of surgery (mn) – Median, IQR	210 (164–258)	206 [160–263]	210 [178–255]	0.62
Blood loss (L) – Median, IQR	1,0 [0,5 − 2,0]	1,0 [0,5 − 2,0]	0,9 [0,4-1.4]	0.81

(Group ≥ 70 year [$n=117$] vs. group <70 year [$n=181$])

Patient demographics and baseline characteristics

We included 298 patients with RCC and IVC thrombus treated at 13 French uro-oncology reference centers between 2007 and 2023. A total of 117 patients were aged over 70 year. Women were more frequently represented in the ≥ 70 year group (38% vs. 24%, $p=0.016$).

The ASA score was significantly higher in the elderly group, whereas the ECOG score was comparable. Preoperative renal function was more impaired in the ≥ 70 year group, with 26 patients (23%) presenting with a GFR <45 mL/min before surgery (vs. 10%, $p<0.01$).

Regarding comorbidities, hypertension, prior thrombotic events (excluding vena cava thrombosis), and anticoagulant use were more prevalent, leading to a significantly higher Charlson Comorbidity Index in the ≥ 70 year group (Table 1).

Disease characteristics

Symptoms at diagnosis were similar between groups. The renal mass was right-sided in 60% of patients. The primary tumor was smaller in the ≥ 70 year group (80 mm [6.1–10.0] vs. 96 mm [7.2–12.0], $p<0.01$).

The thrombus level, classified according to the Klein-Novick classification, was comparable between groups, with 39 (34%) patients in the >70 year group having level III or IV thrombi.

23% of patients over 70 year were staged as cN+, and 24% had metastatic disease (13% lungs, 7% adrenal glands, and 4% brain), which was comparable between groups.

Histological subtypes were similar between groups, with 254 cases (85%) classified as clear-cell RCC.

Therapeutics interventions

All patients underwent surgery as an inclusion criterion. No significant differences were observed in perioperative management. Overall, 16 patients (5%) underwent preoperative biopsy, and 59 patients (20%) underwent preoperative arterial embolization.

Robot-assisted surgery was performed in 13% of cases, and lymph node dissection in 40%. The median estimated blood loss was 1 L (IQR 0.5–2) and surgical time was 210 min, comparable between groups.

Among patients with metastatic disease ($n=72$, 24%), 30% received first-line systemic therapy prior to surgery.

Table 2 Post-operative complications occurring within 90 days

	All ($n=298$)	<70 y ($n=181$)	≥70 y ($n=117$)	p-value
Length of stay (d) - Median, IQR	8 [6–13]	8 [6–13]	8 [6–14]	0.26
Medical complication – n (%)				
Total	120 (40)	63 (35)	57 (49)	0.02
Acute Kidney Injury	36 (12)	19 (10)	17 (15)	0.4
Pneumonia	18 (6)	9 (5)	9 (7)	0.4
Deep Vein Thrombosis	14 (5)	6 (3)	8 (7)	0.2
Paralytic Ileus	15 (5)	7 (4)	8 (7)	0.3
Surgical complications – n (%)				
Total	54 (18)	29 (16)	25 (21)	0.28
Surgical site hematoma	11 (4)	6 (3)	5 (4)	0.8
Surgical site abscess	9 (3)	5 (3)	4 (3)	0.7
Pneumothorax	3 (1)	0	3 (2)	0.06
Reoperation – n (%)	22 (7)	13 (7)	9 (8)	1

Postoperative complications within 90 days (Table 2)

The median length of stay was comparable between groups (<70 year: 8 days [IQR 6–13] vs. ≥70 y: 8 days [IQR 6–14], $p=0.26$). Overall, medical complications occurred in 120 patients (40%), with a significantly higher rate in the ≥70-yr group (49% [57/117] vs. 35% [63/181], $p=0.02$). Acute kidney injury (36 cases, 12%), pneumonia (18 cases, 6%), and paralytic ileus (15 cases, 5%) were the most frequent medical complications, with no significant differences across age groups. Surgical complications occurred in 54 patients (18%), with no significant difference between groups (21% [25/117] vs. 16% [29/181], $p=0.28$). A total of 22 patients (7%) required reoperation, with similar rates in both groups.

Postoperative mortality at 90 days: (Table 3)

At 90 days after surgery, 22 patients (7.4%) had died, including 12/117 (10.3%) in the ≥70-y group and 10/181 (5.5%) in the <70-y group, with no significant difference ($p=0.13$). In the multivariable analysis adjusted for preoperative renal dysfunction, the association did not reach statistical significance (OR 2.1, 95% CI 0.8–5.1, $p=0.14$).

Regarding other preoperative risk factors for 90-d mortality, univariate analysis showed that metastatic disease (OR 3.3, 95% CI 1.4–8.0, $p=0.01$) and preoperative renal dysfunction (OR 3.9, 95% CI 1.2–8.1, $p=0.02$) were significantly associated with increased risk of mortality. In the multivariable model including age and preoperative renal dysfunction, renal dysfunction remained independently associated with mortality (adjusted OR 2.8, 95% CI 1.02–7.1, $p=0.04$).

As an exploratory analysis, a subgroup of patients aged>80 year ($n=32$) was examined. Six patients (19%) died within 90 days, a significantly higher rate than in the <80-yr group ($n=16$, 6%, $p=0.02$).

The 90-day mortality across age categories (<60, 60–70, 70–80, and ≥80 year) did not show a significant increasing trend ($p=0.06$, Fig. 1). However, mortality in the ≥80-yr group appeared higher compared with the three younger categories.

Disease specific survival

Overall survival in the ≥70 year group is presented in Fig. 2 covering up to 10 year post-surgery. The median survival was 85 months (7 year). Overall survival was significantly lower in the ≥70 year group compared to the <70 year group ($p<0.01$).

The disease-specific survival between the ≥70 year and <70 year groups, as shown in Fig. 3, was not statistically different, neither in a univariate model nor after adjustment for sex, eGFR, and ASA score (HR=1.25 [95% CI 0,73−2,13], $p=0.4$).

Discussion

To our knowledge, this study is the largest cohort analyzing the postoperative mortality for renal cell carcinoma surgery with IVC thrombus in the ≥70 year population. Our study

Table 3 Preoperative factor of postoperative mortality within 90 days (univariate and multivariate analysis)

Mortality at 90 d	OR	CI 95%	p	Adjusted OR	CI 95%	p
Age (≥70 yrs)	2.0	0.85–4.9	0.1	2.1	0.8–5.1	0.1
Sex category (Male)	2.0	0.65–6.0	0.2	–	–	–
Left side tumor	1.04	0.4–2.5	0.9	–	–	–
Type of thrombus (Level 3 & 4)	0.9	0.4–2.3	0.8	–	–	–
Metastatic disease	3.3	1.4-8	0.01	–	–	–
Hypertension	1.1	0.5–2.6	0.8	–	–	–
Obesity (BMI>30)	0.9	0.3–2.7	0.8	–	–	–
High ASA score (3 & 4)	1.3	0.7–4.1	0.3	–	–	–
Anticoagulant	1.9	0.7-5	0.2	–	–	–
Preoperative renal dysfunction (eGFR<45)	3.9	1.2–8.1	0.02	2.8	1.02–7.1	0.04

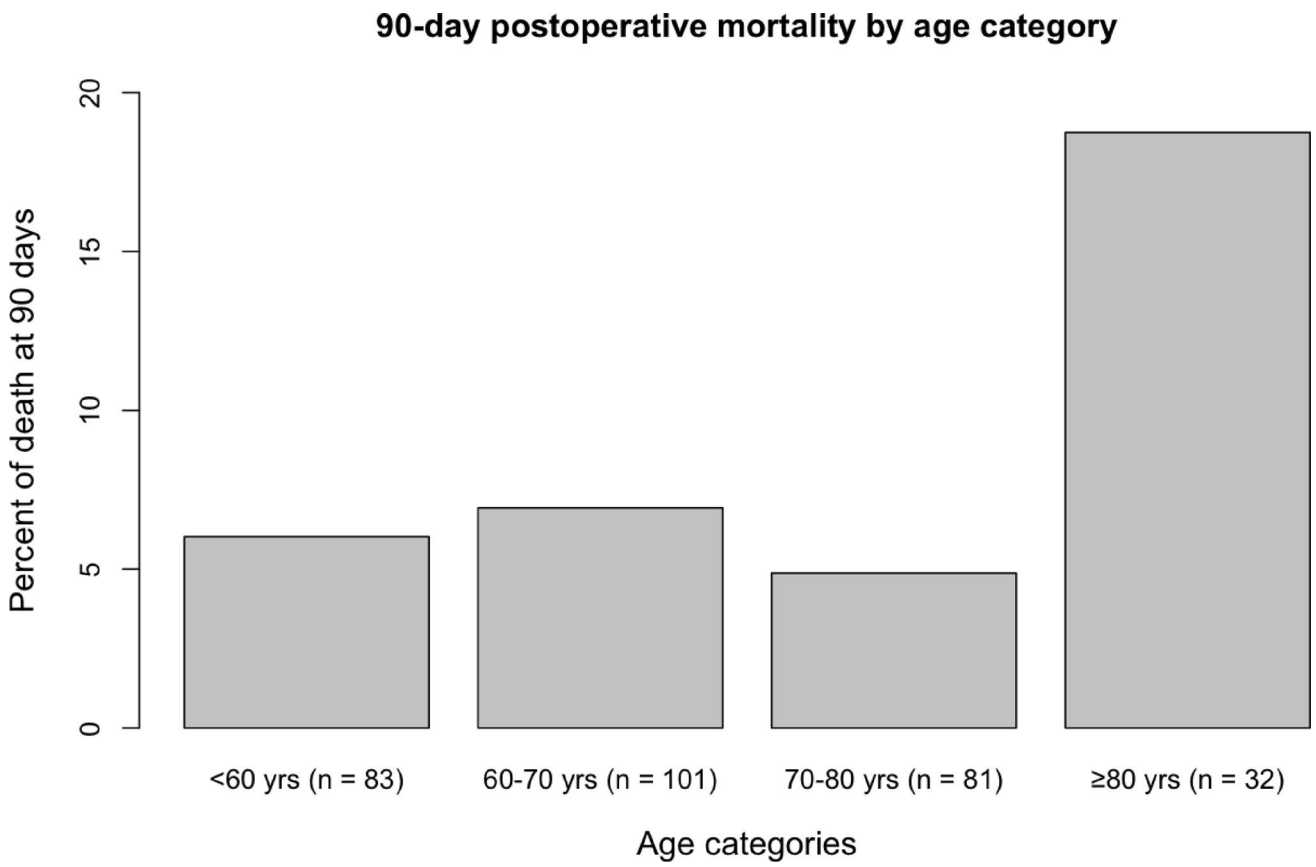

Fig. 1 Distribution of ninety-days postoperative mortality according to age categories. * Chi-squared test for trend, $p=0.06$

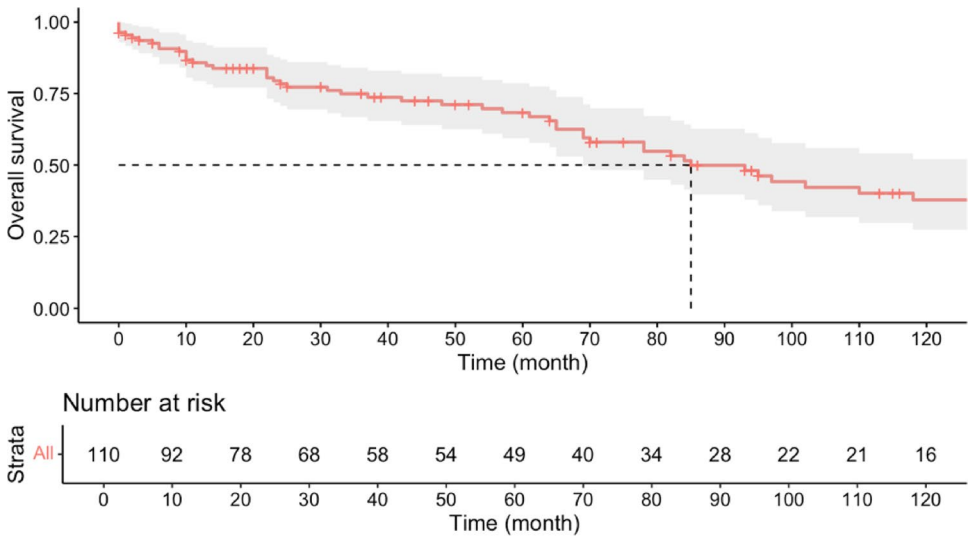

Fig. 2 Overall Survival in the ≥70 y group. *Median overall survival = 85 months

did not demonstrate a significant increase in postoperative mortality in patients older than 70 year treated for RCC associated with an IVC thrombus.

This finding is consistent with previously published literature. In the study by Ishiyama et al. [8], results were similar despite the inclusion of fewer patients. We hypothesize that the 70 year threshold may be too low; our exploratory analysis in patients aged ≥ 80 year found a statistically significant increase in 90-day postoperative mortality, though the small sample size ($n=32$) restricts the strength of this conclusion. Similarly, Martin et al. [7] reported an OR of 2.14 ($p=0.029$) for in-hospital mortality in the 70–79 year group and 5.81 ($p<0.01$) in those aged ≥ 80 year compared to patients aged < 50 year, corroborating our findings. Their

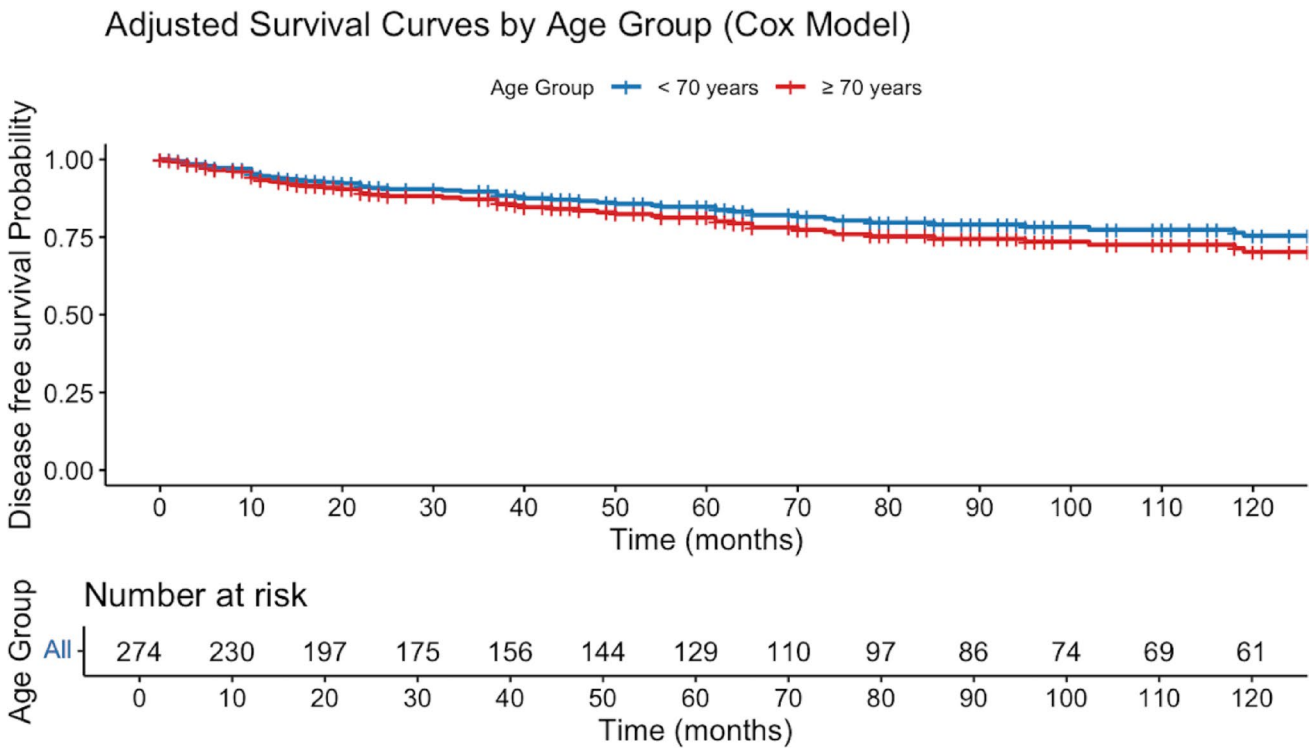

Fig. 3 Disease-specific survival multivariate analyses **(**Adjusted model on eGFR, sex and ASA score). Multivariate analysis performed using Cox proportional hazards regression.*HR = 1.25 [95% CI 0,73 − 2,13], $p = 0.4$

larger sample size of over 3,000 patients in their study provided superior statistical power. These results underscore the importance of caution in surgical decision-making.

Renal dysfunction (eGFR < 45 mL/min) is a preoperative predictor of 90-day mortality, regardless of patient age. Several studies have reported a marked increase in postoperative mortality below this threshold, independent of the surgical procedure. [9, 10] Zagar et al. reported a higher incidence of postoperative medical complications in patients with chronic kidney disease, defined as a GFR < 60 mL/min, following nephrectomy and thrombectomy [11]. 1In the context of nephrectomy and prolonged surgery with bleeding, this information should play a central role in preoperative decision-making, and severe postoperative acute renal failure management may be anticipated to reduce medical complications and limit the associated increase in morbidity and mortality [12].

Patients with metastatic disease exhibited a higher 90-day postoperative mortality rate. This increased postoperative mortality has been well documented in series focusing on nephrectomy alone [13–15]. Metastatic status could not be included in the multivariable model due to the limited number of events ($n = 22$). This restriction of the model to preoperative renal dysfunction represents a clear limitation and requires cautious interpretation of the results. However, the proportion of metastatic cases did not differ significantly between groups, thereby minimizing its potential impact on the logistic regression analysis. Nonetheless, additional potential confounders may not have been incorporated.

Although this study is retrospective, the use of the prospectively included national UroCCR cohort allowed for detailed patient characterization with a low rate of missing data. Notably, sex-ratio differed between younger and older groups, showing a statistically higher proportion of female patients in the ≥ 70 year group—a finding not previously reported. This may be explained by the longer life expectancy of women and a better ASA score, leading to a higher proportion of older women being eligible for surgery. Additionally, tumors were smaller in the ≥ 70 year group, a finding not reported in prior studies [7, 8]. A potential limitation is that only operable patients were included, which may have excluded individuals with larger tumors deemed unfit for surgery, particularly those > 70 year, which may partly explain the difference in median tumor size between groups.

In addition, although our study is limited to France, it draws on data from 13 expert centers across diverse regions, thus enhancing the representativeness of the cohort. Nonetheless, the study population is restricted to high-volume centers, which are known to be associated with lower postoperative mortality [7]. Moreover, variations in surgical expertise, perioperative management protocols, and postoperative care—such as the use of preoperative embolization, robot-assisted approaches, or systemic therapy—may have influenced the outcomes [16].

Furthermore, our study presents long-term oncological outcomes, with a median overall survival of 85 months in the ≥70 year group, which appears slightly longer than that reported in previous series [8, 17–19]. This favorable outcome may be explained by recent advances in systemic therapies and the management of patients in expert centers. The retrospective nature of our study may have introduced attrition bias; however, the low rate of losses to follow-up strengthens the reliability of our findings. Additionally, contrary to overall survival, disease-specific mortality appears comparable between age groups, consistent with the results reported by Ishiyama et al. [8]. These results may encourage the consideration of interventional therapies in ≥70 year patients, provided that the critical 90-day postoperative period is safely managed, as the disease does not appear to exhibit more aggressive behavior compared to younger individuals. Neo-adjuvant systemic therapy in non-metastatic patients should also be evaluated in clinical trials, in order to allow for lower IVC thrombus level, potentially allowing for less complex surgery [20].

Further prospective studies are needed to better stratify surgical candidates among the ≥70 year group, incorporating comprehensive geriatric assessments, patient preferences, and alternative treatment modalities. Ultimately, multidisciplinary discussions should be encouraged to optimize individualized treatment strategies, particularly for patients over 80 year.

Conclusion

In conclusion, radical nephrectomy with vena cava thrombus extraction in ≥70 year patients yields acceptable perioperative and oncological outcomes, comparable to those observed in patients aged<70 year. Although postoperative mortality does not significantly increase in patients aged≥70 year, a markedly higher 90-day mortality rate is observed in patients aged≥80 year, underscoring the importance of careful patient selection. Our findings highlight the need to incorporate preoperative renal function and comorbidities, notably impaired eGFR, into the surgical decision-making process. Given the comparable long-term DSS in elderly patients, surgical intervention may remain a valuable option, provided perioperative risks are carefully assessed.

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Declarations.

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest All authors declare that they have no relevant financial or non-financial interests to disclose.

Ethical approval This study was conducted in accordance with institutional and ethical guidelines as part of the UroCCR project (NCT03293563), which received IRB "Comité de Protection des Personnes Sud-Ouest et Outre-mer III" approval and authorization from the French Data Protection Authority (CNIL, DR-2013-206). Decision no. DT-2024-027 (December 31, 2024) authorized the Bordeaux University Hospital Center to implement the UroCCR health data warehouse.

Consent to participate Written informed consent was obtained from all patients included in the UroCCR project.

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