

# Role of Histology in Influencing Outcomes after Cytoreductive Nephrectomy for Metastatic Renal Cell Carcinoma



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## Introduction

- Cytoreductive nephrectomy (CN) benefits: removing primary tumor, minimizing risk of de novo metastases, alleviating paraneoplastic symptoms, obtaining histological diagnoses.
- CN risks: perioperative morbidity and mortality, delayed or interrupted systemic therapies.
- Early studies: survival benefit of CN + systemic therapies; role of CN challenged by recent phase III CARMENA trial.
- Role and timing of CN for patients with metastatic RCC (mRCC) remains a moving target.
- Clear Cell RCC (ccRCC) = 70% of all RCCs
- Evidence for CN in patients with non-ccRCC (nccRCC) remains scarce.
- We lack comparative safety and efficacy studies of CN for ccRCC versus nccRCC histology.

## Objective

We sought to characterize perioperative and survival outcomes among patients who underwent CN for mRCC based on their histologic subtype.

## Methods

- We reviewed our institutional registry of patients who underwent nephrectomy between 1996 and 2021.
- Patients undergoing CN were stratified by histologic subtype and grouped as either ccRCC or nccRCC.
- Presence and extent of tumor thrombus was graded according to the Mayo Clinic Grading System.
- Perioperative outcomes, including estimated blood loss (EBL), hospital length of stay (LOS), intraoperative or postoperative complications, and 90-day readmission rates were assessed.
- Postoperative complications were graded according to the Clavien-Dindo classification.
- Appropriate statistical tests were conducted using Stata 17.0.

## Results

**Table 1: Baseline clinicopathologic characteristics of patients that underwent CN stratified by histology subtype.**

Factor	Value	Clear Cell (126)	Non-Clear Cell (29)	P-value
Race	White	117 (92.9%)	21 (72.4%)	<0.001
	Asian	5 (4.0%)	0 (0.0%)	
	Black	4 (3.2%)	8 (27.6%)	
CCI, median (IQR)		8 (7, 9)	8 (6, 9)	0.68
Preoperative Symptoms	No	29 (23.0%)	4 (13.8%)	0.02
	Yes	27 (21.4%)	15 (51.7%)	
	Unknown	70 (55.6%)	10 (34.5%)	
Clinical N Stage	cN0	82 (65.1%)	12 (41.4%)	0.062
	cN1	39 (31.0%)	15 (51.7%)	
	cNx	5 (4.0%)	2 (6.9%)	
Pathological Stage Classification	pT1	9 (7.1%)	4 (13.8%)	0.046
	pT2	15 (11.9%)	6 (20.7%)	
	pT3	94 (74.6%)	14 (48.3%)	
	pT4	6 (4.8%)	4 (13.8%)	
	Unknown	2 (1.6%)	1 (3.4%)	
Sarcomatoid Features	No	108 (85.7%)	25 (86.2%)	0.81
	Yes	15 (11.9%)	4 (13.8%)	
	Unknown	3 (2.4%)	0 (0.0%)	
Rhabdoid Features	No	42 (33.3%)	11 (37.9%)	0.27
	Yes	12 (9.5%)	1 (3.4%)	
	Unknown	72 (57.1%)	17 (58.6%)	
Systemic Therapy Received	No	32 (25.4%)	15 (51.7%)	0.006
	Yes	93 (73.8%)	14 (48.3%)	
	Unknown	1 (0.8%)	0 (0.0%)	
Timing of Systemic Therapy if Received	Pre-CN	3 (3.0%)	2 (14.0%)	0.16
	Post-CN	88 (94.0%)	12 (86.0%)	
	Unknown	3 (3.0%)	0 (0.0%)	
Metastatic Sites	1	58 (46.0%)	12 (41.4%)	0.55
	2	44 (34.9%)	12 (41.4%)	
	3	20 (15.9%)	2 (6.9%)	
	4	2 (1.6%)	0 (0.0%)	
	Unknown	2 (1.6%)	3 (10.3%)	

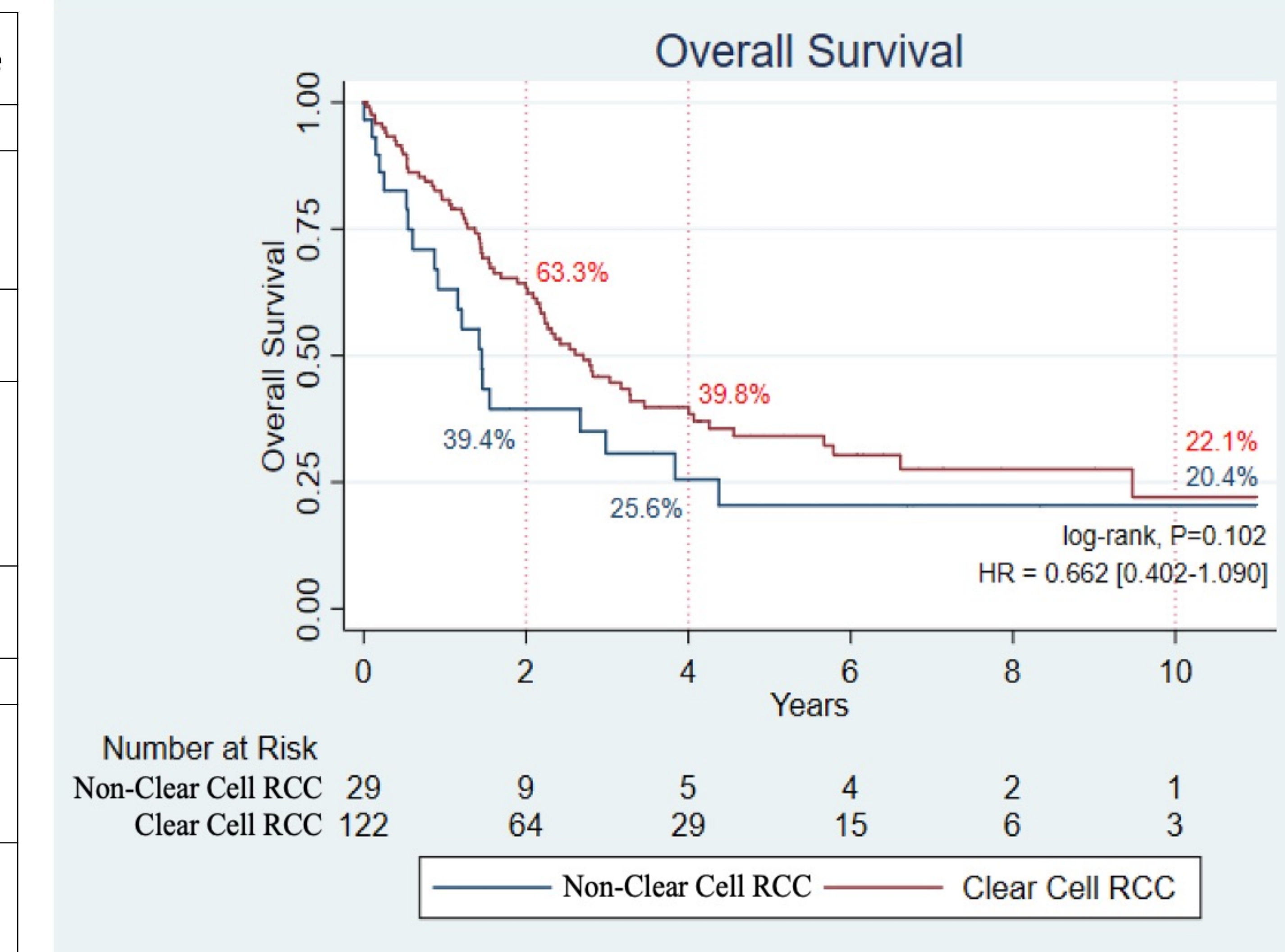
**Table 2: Perioperative and postoperative outcomes following CN stratified by histologic subtype.**

Factor	Level	Clear Cell (126)	Non-Clear Cell (29)	P-value
<b>Perioperative Outcomes</b>				
Approach	Minimally Invasive	72 (57.1%)	18 (62.1%)	0.63
	Open	54 (42.9%)	11 (37.9%)	
EBL (mL), median (IQR)		300 (100,999)	999 (200,999)	0.20
Intraoperative Complication	No	112 (88.9%)	28 (96.6%)	1.00
	Yes	7 (5.6%)	1 (3.4%)	
	Unknown	7 (5.6%)	0 (0%)	
Median LOS, days (IQR)		4 (2, 6)	4 (2, 6)	0.59
<b>Postoperative Outcomes</b>				
Postoperative Complication	No	105 (83.3%)	24 (82.8%)	1.00
	Yes	21 (16.7%)	5 (17.2%)	
Clavien-Dindo Classification	Grade I	8 (38%)	0 (0%)	0.10
	Grade II	6 (29%)	2 (40%)	
	Grade IIIa	4 (19%)	0 (0%)	
	Grade IIIb	1 (5%)	0 (0%)	
	Grade IVa	1 (5%)	1 (20%)	
	Grade IVb	0 (0%)	1 (20%)	
90-day Readmission	No	113 (89.7%)	23 (79.3%)	0.28
	Yes	4 (3.2%)	2 (6.9%)	
	Unknown	9 (7.1%)	4 (13.8%)	

## Conclusions

- nccRCC histology does not negatively impact survival outcomes after CN for mRCC compared to those with ccRCC
- Patient selection remains paramount to determine eligibility for CN → histologic subtype should not be an exclusionary factor when performing CN at high-volume, experienced centers.

**Figure 1: Overall survival of patients after CN stratified by histology subtype.**



**Table 3: Multivariable Cox regression analysis for worse OS after CN.**

Factor	Level	HR	95% CI	P-Value
Histology	Clear Cell		Reference	
	Non-Clear Cell	1.344	0.697 – 2.592	0.378
CCI		1.112	0.960 – 1.288	0.158
Path. Stage Classification	pT1		Reference	
	pT2	3.068	1.047 – 8.989	0.041
	pT3	1.611	0.604 – 4.296	0.341
	pT4	3.549	0.914 – 13.775	0.067
Presence and Extent Of Tumor Thrombus	None		Reference	
	Level I	1.132	0.543 – 2.358	0.741
	Level II	0.561	0.282 – 1.116	0.099
	Level III	1.141	0.572 – 2.278	0.708
	Level IV	Insuff.	-	-
Sarcomatoid Features	No		Reference	
	Yes	2.152	1.106 – 4.188	0.024
Systemic Therapy Received	No		Reference	
	Yes	0.960	0.505 – 1.825	0.902
Metastatic Sites	1		Reference	
	2	1.255	0.723 – 2.179	0.419
	3	2.018	1.009 – 4.034	0.047
	≥4	1.868	0.406 – 8.603	0.422

**Take Away: Given limited effective systemic treatment options for patients with nccRCC, CN likely maintains an important role for appropriately selected patients with metastatic nccRCC.**