Outcomes of Surveillance following Cytoreductive Nephrectomy in Metastatic Renal Cell Carcinoma

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Introduction and Objectives

•The CARMENA trial demonstrated that sunitinib alone was non-inferior to cytoreductive nephrectomy (CN) followed by sunitinib with regard to overall survival (OS) for patients with metastatic renal cell carcinoma (mRCC).

•However, as CARMENA focused on patients requiring systemic therapy; the role of CN for patients not treated with upfront systemic therapy remain unknown.

•We sought to describe the oncologic outcomes of patients with de-novo synchronous mRCC who underwent CN and initial surveillance, with or without metastasis-directed therapy (MDT), and without planned immediate postoperative systemic therapy.

Materials and Methods

•We identified 156 adults in the Mayo Clinic Nephrectomy Registry who underwent upfront CN for unilateral, sporadic, mRCC between 1996 and 2016 without postoperative systemic therapy within 3 months of CN.

•Metastases documented at nephrectomy were managed with initial surveillance or MDTs including metastasectomy, radiation, radio-frequency ablation, or cryoablation within 3 months of CN

•The co-primary outcomes were (i) systemic therapy-free survival (STFS) and (ii) OS, measured from 3-months post-CN. Features associated with STFS and OS were assessed using multivariable Cox-regression models with best subsets selection.

Results

•115 patients (74%) had a single metastatic site. 37 (24%) patients were managed after CN with surveillance alone and 119 (76%) underwent MDT, of whom was complete in 77 (49%) 72 patients initiated systemic therapy at a median of 0.7 years

•The median follow-up among survivors was 6.2 years

•STFS rates at 1, 3, and 5 years were 47%, 21% and 14%

•OS rates at 1, 3, and 5 years were 69%, 37%, and 28%

•On multivariable analysis, having multiple metastatic sites was associated with worse STFS (HR 1.85; 95%CI 1.25-2.73; p=0.002), while complete metastasectomy was associated with improved OS (HR 0.59; 95%CI 0.40-0.87; p=0.008)

Table 1: Multivariate Model for Systemic Therapy Free Survival

Feature	HR (95% CI)	P-value
Post-cytokine era (2006-2016)	0.53 (0.36-0.77)	0.001
Multiple metastatic sites at nephrectomy	1.85 (1.25-2.73)	0.002
Grade*		
1, 2	1.0 (reference)	
3	1.59 (1.01-2.50)	0.04
4	3.29 (1.87-5.77)	<0.001

*Grade not assigned to chromophobe RCC.

Table 2: Multivariate Model for Overall Survival

Feature	HR (95% CI)	P-value
Post-cytokine era (2006-2016)	0.42 (0.28-0.64)	<0.001
Low hemoglobin	1.92 (1.31-2.81)	<0.001
ECOG performance status*	1.61 (1.22-2.14)	<0.001
Grade†		
1, 2	1.0 (reference)	
3	0.85 (0.53-1.34)	0.5
4	2.19 (1.25-3.85)	0.006
Upfront complete metastasectomy	0.59 (0.40-0.87)	0.008

*HR and CI represent a 1-unit increase in ECOG performance status.
†Grade not assigned to chromophobe RCC.

Conclusion

•Among appropriately selected patients managed with surveillance or MDT after CN, approximately half are estimated to be alive and not requiring systemic therapy at one year, with a subset achieving long term STFS.

•Having a single metastatic site and disease amenable to complete metastasectomy are features associated with improved STFS and OS after upfront CN.

•These data may help select which patients may be well served with upfront CN.