DOES PRESENCE OF BONE METASTASES PORTEND WORSENED PROGNOSIS IN RENAL CELL CARCINOMA? ANALYSIS OF THE REMARCC (REgistry of MetAstatic RCC) DATABASE

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INTRODUCTION/OBJECTIVES

- The presence of brain metastases and bone metastases are generally understood to herald worsened prognosis following nephrectomy in patients with renal cell carcinoma (RCC).
- We sought to determine the effect of bone metastases on mortality and oncologic outcomes when already present at the time of cytoreductive radical nephrectomy (RN).

METHODS

- Multicenter retrospective analysis of mRCC patients from the (REgistry of MetAstatic RCC) REMARCC database.
- Demographics, clinical variables, and outcomes were collected.
- Patients were stratified into low, medium, and high-risk groups based on MSKCC/Motzer Criteria.
- Analysis of impact of bone metastases was conducted overall and within each risk group utilizing Kaplan-Meier analysis (KMA).
- Multivariable analysis (MVA) was utilized to identify predictors for outcomes.
- Primary outcome was progression-free survival (PFS) and secondary outcome was overall survival (OS).

Table 1: Clinical Descriptives and Tumor Characteristics

Variable	All, n=447	Bone Mets, n=124	No Bone, n=323	*p-value*
Age (mean +/- std dev)	61.9 +/- 12.0	62.1 +/- 9.9	61.8 +/- 12.7	*0.824*
Sex (male) n (%)	311 (69.6)	88 (80.0)	223 (69.0)	*0.692*
BMI (mean +/- std dev)	26.6 +/- 5.0	27.0 +/- 5.2	26.5 +/- 5.0	*0.464*
Clin Tumor stage, n (%)	1- 66 (15.5) 2- 110 (25.8) 3- 214 (50.1) 4- 37 (8.3)	1- 29 (25.7) 2- 32 (28.3) 3- 49 (43.4) 4- 3 (2.7)	1- 37 (11.8) 2- 78 (24.8) 3- 165 (52.5) 4- 34 (10.8)	***<0.001***
Clin Node status (positive), n (%)	180 (46.2)	46 (39.7)	134 (42.3)	*0.062*
ECOG (mean +/- std dev)	0.95 +/- 1.0	1.0 +/- 1.1	0.93 +/- 1.0	*0.503*
Path tumor size in cm (mean +/- std dev)	11.46 +/- 14.8	9.6 +/- 11.1	12.2 +/- 16.0	*0.057*
Pathology, n (%)	Clear Cell- 358 (81.0) Papillary- 46 (10.4) Chromophobe- 10 (2.3) Other- 28 (6.3)	CC- 93 (75.6) P- 19 (15.4) Ch- 3 (2.4) Other- 8 (6.5)	CC- 265 (82.8) P- 27 (8.4) Ch- 7 (2.2) Other- 20 (6.3)	*0.268*
Sarcomatoid differentation (positive), n (%)	76 (18.1)	20 (16.5)	56 (18.7)	*0.596*

Table 2: Procedural Variables and Outcomes

Variable	All, n=447	Bone Mets, n=124	No Bone, n=323	*p-value*
EBL (mL) (mean +/- std dev)	631.3 +/- 1003.9	471.6 +/- 601.8	694.2 +/- 1118.6	***0.034***
Positive Surgical Margins, n (%)	49 (12.2)	13 (11.0)	36 (12.7)	*0.643*
Pathological Upstaging, n (%)	105 (24.5)	37 (32.7)	68 (21.1)	***0.014***
Length of Stay (mean +/- std dev)	9.3 +/- 8.1	9.0 +/- 8.2	9.4 +/- 8.1	*0.633*
Intra-op Comp, n (%)	80 (18.5)	18 (14.9)	62 (19.9)	*0.224*
Post-op clavien 3+, n (%)	29 (6.5)	5 (4.0)	24 (7.4)	*0.623*
30 d Readmission, n (%)	27 (7.3)	10 (9.8)	17 (6.3)	*0.245*
NED after Primary tx, n (%)	28 (12.7)	8 (13.1)	20 (12.6)	*0.915*
Metastatectomy, n (%)	99 (22.1)	37 (29.8)	62 (19.2)	***0.015***
Length of Follow Up	14.1 mo median, std dev 24.7 mo	24.8 mean, 27.3 std dv	22.1 mean, 23.6 std dv	*0.348*
Alive at last F/u, n (%)	186 (43.1)	49 (40.5)	137 (44.1)	*0.503*

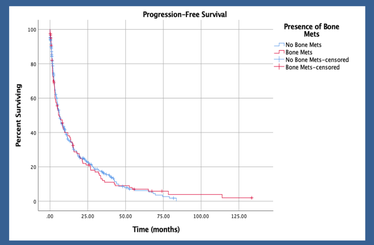
Table 3: Risk Group Stratification

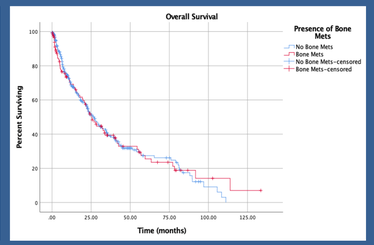
Metastases Present	Total	Low Risk	Intermediate risk	High risk
All	361 (of 447)	30, 8.3%	208, 57.6%	123, 34.1%
Bone Mets	95 (of 124)	6, 6.3%	55, 57.9%	34, 35.8%
No Bone Mets	266 (of 323)	24, 9.0%	153, 57.5%	89, 33.5%

Table 4: Multivariate Analysis

Progression Free Survival			
Variable	**Hazard Ratio**	**95% CI**	***p-value***
Age (increasing)	1.001	0.991 – 1.012	*0.811*
Sex (Male)	0.950	0.740 – 1.219	*0.685*
Presence of Bone Mets	1.053	0.818 – 1.355	*0.690*
Motzer Int Risk (Low Risk Referent)	1.889	1.197 – 2.982	***0.006***
Motzer High Risk (Low Risk Referent)	3.238	2.014 – 5.205	***<0.001***
Overall Survival			
Variable	**Hazard Ratio**	**95% CI**	***p-value***
Age (increasing)	1.001	0.991 – 1.012	*0.817*
Sex (Male)	0.966	0.752 – 1.240	*0.785*
Presence of Bone Mets	1.002	0.779 – 1.288	*0.990*
Motzer Int or High Risk (Low Risk Referent)	2.227	1.424 – 3.482	***<0.001***

Figures 1a and 1b: PFS and OS for Bone Metastases vs. None





Figures 2a-d: PFS and OS for Bone Metastases vs. None when stratified by Motzer Group (Intermediate or High Risk)

Fig 2a. PFS In Int. Risk p=0.786

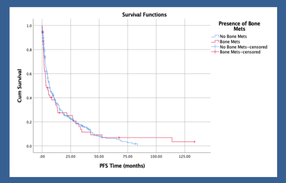


Fig 2b.OS in Int. Risk p=0.365

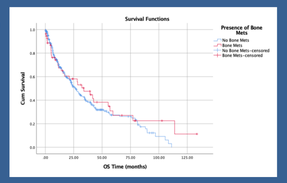


Fig 2c.PFS in High Risk p=0.487

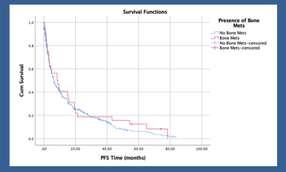
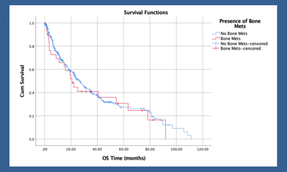


Fig 2d.OS in High Risk p=0.558



RESULTS

- A total of 447 patients were included in the initial analysis, and a total of 361 patients were stratified according to MSKCC/Motzer Risk criteria (low- n=30, intermediate- n=208, and high-risk mRCC n=123, median follow-up 14.3 months).
- 124 patients had bone metastases and 323 had mRCC but no bone metastases. No significant demographic differences were noted between groups.

MVA

- MVA for PFS demonstrated increasing Motzer risk categories as independent predictors.
- MVA for OS revealed higher Motzer risk category as independently predictive.
- In neither analysis was presence of bone metastases significant (PFS p=0.690, OS p=0.268).

KMA

- KMA showed no difference in median PFS for bone metastases vs. non bone metastases groups (Fig 1a, 6.1 vs. 6.4 months, p=0.973)
- KMA showed no difference in median OS (Fig 1b, 25.5 vs. 26.5 months, p=0.958).
- Stratification of patients into different MSKCC/Motzer risk categories did not demonstrate difference between bone vs. none bone mRCC for PFS and OS.

CONCLUSIONS

- Presence of bone metastases does not independently affect survival or oncologic outcomes in mRCC.
- The prognostic significance of bone metastases may be less than previously hypothesized.