

PAPER 33

Metastatic Bone Disease at Diagnosis is Associated with Increased Rate of Body Mass Index Loss and Worse Survival in Clear Cell Renal Cell Carcinoma

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Background: Metastatic bone disease in animal models drives increased cachexia, a muscle-wasting syndrome common in cancer and responsible for 20 to 40% of cancer-related deaths. However, the impact of metastatic bone disease on cachexia has not been extensively characterized in human cancer patients. Clear cell renal cell carcinoma (CCRCC) frequently metastasizes to bone and 40% of patients with CCRCC develop cachexia. Biometric measures such as Body Mass Index (BMI), are indicators of cachectic progression. To best manage patients in the future, an improved understanding of the systemic consequences of metastatic bone disease is needed.

Questions/purposes: Does the presence of osseous metastatic disease, compared to localized or extraosseous disease predict BMI at diagnosis and change in BMI over time in CCRCC? Is overall survival worse in CCRCC patients who present with Osseous metastatic disease, compared to those with localized or extraosseous disease at presentation?

Methods: CCRCC patients who were treated between 2010 and 2019 were retrospectively identified from an institutional database. Patients at least 18 years of age with greater than 2 years follow-up were included. Patients with incomplete medical documentation, follow-up, or body metrics were excluded. Patients who met inclusion and exclusion criteria were assigned to one of three cohorts at diagnosis: those with *Local* disease only (Stage II and III combined), those with *Extraosseous* metastatic disease (no metastatic site in bone), and those with *Osseous* metastatic disease (must include at least one metastatic site in bone). Patient height and weight within three months of diagnosis and at last known follow-up were recorded. Total follow-up for BMI was determined using date of diagnosis and date of last body metric recording. Survival data was extracted from the institutional database, which is updated at least annually. Rate of change in BMI per year was determined and compared between groups using Kruskal-Wallis Test with Dunn's post-hoc for multiple comparisons. Kaplan-Meier analysis was performed, and survival compared using a pairwise log-rank test.

Results: Patients with *Local* disease had a median BMI at diagnosis of 31.48 (IQR:26.53-38.38) compared to those with *Extraosseous* (28.40; IQR:25.03-32.98; $p=0.0514$) and *Osseous disease* (27.64; IQR:24.17-32.35; $p=0.0046$) (**Figure 1A**). Change in BMI for *Local* disease was 0.5700% per year (IQR: -1.534-2.521) compared to *Extraosseous* (-1.777% per year; IQR: -9.949-2.040; $p=0.06$) and *Osseous disease* (-3.752% per year; IQR: -13.26-2.055; $p=0.01$) (**Figure 1B**). Survival at 1-year for *Local* disease was 90.1% [95% CI: 84.4%-96.1%], 70.8% [95% CI: 62.4%-80.3%] for *Extraosseous* disease, and 56.1% [95% CI: 47.9%-67.1%] for *Osseous disease*. Survival over 5 years was not significantly different between *Extraosseous* and *Osseous disease* ($p=0.36$), but both were significantly different compared to *Local* disease survival ($p<0.001$ for both disease states) (**Figure 1C**).

Conclusions: We present a retrospective study on the impact of metastatic bone disease on BMI at diagnosis and over time in patients with CCRCC. In this analysis, *Osseous* metastatic disease was associated with significantly lower BMI at diagnosis and decrease in BMI over time, compared to *Local* disease. Similar but notably smaller trends were observed between *Extraosseous* metastatic disease and *Local* disease. No significant differences were identified between *Osseous* and *Extraosseous* disease, though we believe our study was likely underpowered to discriminate between these groups, particularly given large difference in survival at one year. Overall, these findings merit further investigation into the association between osseous metastatic disease, cachexia, and survival. Future studies will evaluate quantitative imaging-based measures of body composition and cachexia in this cohort.

Level of evidence: Retrospective case-control study, Level III evidence

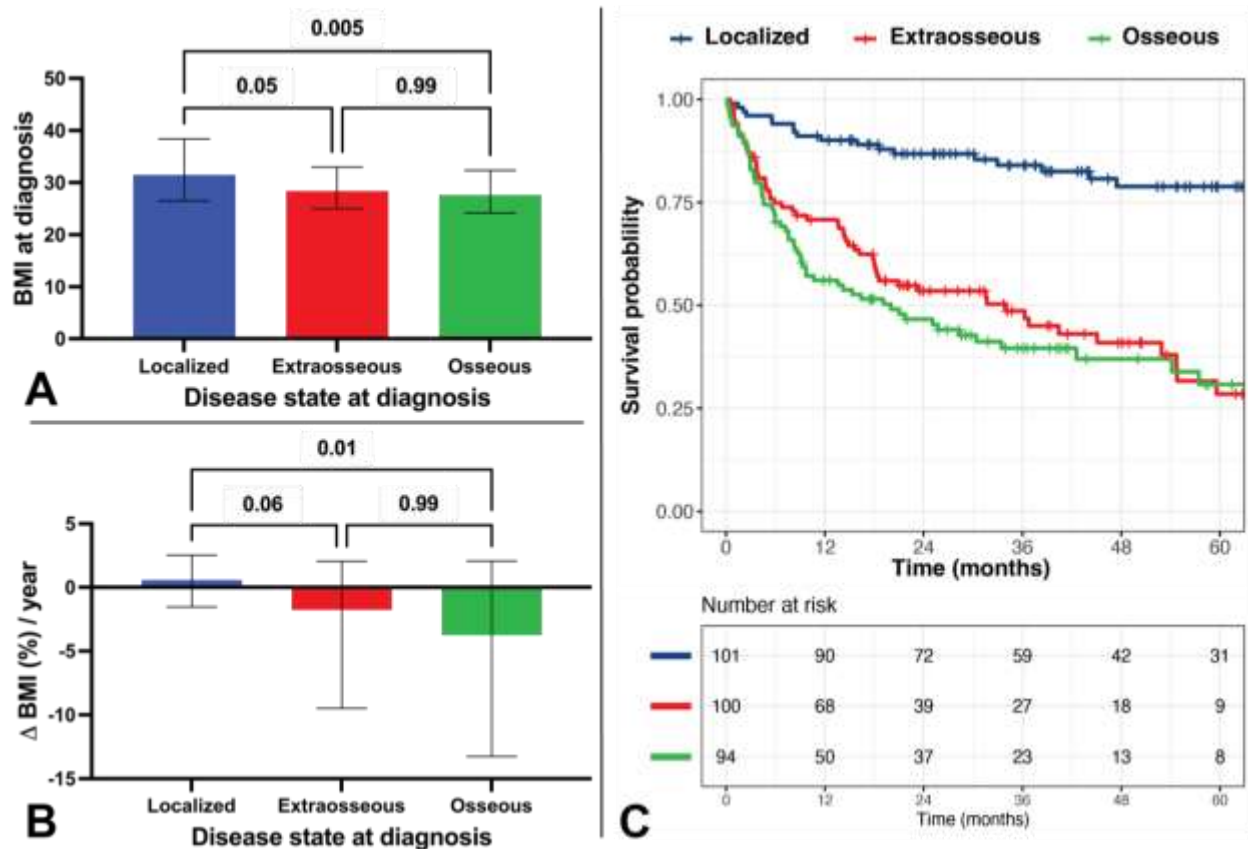


Figure 1. Comparison of body mass index (BMI) and survival in clear cell renal cell carcinoma patients with *Local*, *Extrasosseous* metastatic disease, and *Osseous* metastatic disease at diagnosis. BMI at diagnosis (**A**) and over time (**B**) are shown as median values with interquartile range. Kaplan-Meier survival analysis is shown in **C**. p-value less than 0.05 is significant.