Cureus

Clinical Outcomes of Intracranial Radiosurgery for Brain Metastases in Clear Cell and Non-Clear Cell Renal Cell Carcinoma Patients

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Abstract
Published 02/11/2022

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Categories: Medical Physics, Radiation Oncology
Keywords: stereotactic radiosurgery, brain metastases, renal cancer

How to cite this abstract
Ma J, Del Balzo L, Flynn J, et al. (February 11, 2022) Clinical Outcomes of Intracranial Radiosurgery for Brain Metastases in Clear Cell and Non-Clear Cell Renal Cell Carcinoma Patients. Cureus 14(2): a743

Abstract

Objective: Modern therapeutics for renal cell carcinoma (RCC) such as immunotherapy (IO) and targeted biologics have led to significant improvements in systemic control and overall survival, making the effective management of brain metastases (BM) a critical and frequent problem. Patients with active BMs have often been excluded from contemporary RCC clinical trials, and thus there is limited literature on the management of RCC BM with SRS and novel therapeutics, particularly among RCC patients with non-clear cell histologies. Thus, in the present work, we have sought to evaluate clinical outcomes following SRS in patients with clear cell (ccRCC) and non-clear cell RCC BM in a contemporary cohort of patients.

Methods: We performed a single-institution retrospective analysis of histologically-confirmed renal cell carcinoma patients with parenchymal brain metastases treated with SRS from 2010-2021. We excluded patients with calvarial metastases or patients without baseline intracranial imaging available. We obtained patient demographics and treatment characteristics from medical record review including systemic therapy agents and duration, Karnofsky performance status (KPS), baseline neurological status, RCC histologic subtype, and extent of systemic disease. Systemic disease control at time of BM diagnosis was defined as the absence of new or progressive disease on imaging <2 months from diagnosis of BM. Volumetric data was obtained from SRS plans and tumor diameter was measured using contrast-enhanced MRI imaging at baseline and follow-up. Univariable and multivariable analyses were performed for the endpoints of overall survival (OS) and intracranial progression-free survival (iPFS) using Cox proportional hazards models. iPFS is defined as the duration from time of BM diagnosis to the development of new parenchymal brain metastases, local recurrence, leptomeningeal disease, or death.

Results: We identified 95 patients including 78 (82%) with ccRCC and 17 (18%) with non-ccRCC who received 233 courses of SRS. Median follow-up was 37.3 months. Median iPFS was 8.4 months overall, with 9.4 months for ccRCC and 8.3 for non-ccRCC patients. Median OS was 19 months overall, with 21 months for ccRCC and 14 for non-RCC. Median SRS dose was 21Gy (range: 16-30) and median number of fractions was 1 (range: 1-5). Median PTV overall was 1.34cc (range: 0.08-188), with median PTV of 1.38cc for ccRCC and 1.92cc for non-ccRCC patients. Median tumor diameter was 8.9mm (range: 1-64) including median of 8.0mm for ccRCC and 9.9mm for non-ccRCC patients. Twenty-one (9%) lesions were resected and treated with post-operative SRS, including 17 ccRCC and 3 non-ccRCC patients. Fifty-eight patients (61%) had KPS ≤80 and 92% had extracranial metastases, of which 36% had controlled systemic disease. Sixty-one (65%) patients presented with neurologic symptoms at the time of BM diagnosis. There was no intracranial progression of treated lesions or development of new intracranial mets in 38 ccRCC patients and 13 non-cc RCC patients. On univariable analysis, only non-controlled systemic disease (HR 1.74; p=0.028) was associated with iPFS, and with no variables significantly associated with iPFS on multivariable analysis. Univariable OS analysis revealed that only KPS >80 was associated with overall survival (HR 0.54, p=-0.021), with a trend towards significance for uncontrolled extracranial disease (HR 1.68, p=0.057) and non-ccRCC histology (HR 1.73; p=0.11). Multivariable analysis demonstrated both KPS >80 (HR 0.52, p=0.014) and uncontrolled extracranial disease (HR 1.77, p=0.037) were independently associated with OS.

Conclusion: To our knowledge, this is the first study comparing outcomes of SRS for ccRCC and non-ccRCC histologies in a modern cohort of patients. Our results suggest that SRS is an effective treatment for ccRCC while its role in the treatment of non-ccRCC is less clearly delineated. Further evaluation of RCC patients with BM is warranted, particularly those with non-clear cell histologies. Future molecular analyses may

identify putative biomarkers and guide a precision medicine approach to the treatment of RCC BM.