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Original research article

CyberKnife Stereotactic Radiosurgery in brain metastases: A report from Latin America with literature review

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ABSTRACT

Background and aim: Stereotactic radiosurgery is increasingly being employed for the treatment of brain metastases, both as an adjuvant to surgical resection, and also as a primary treatment modality. The aim of this study is to evaluate overall survival and local control in patients with brain metastases treated with CyberKnife Stereotactic Radiosurgery (CKRS), due to the lack of evidence reported in Latin America.

Materials and methods: We performed a retrospective chart review from October 2011 to January 2017 of 49 patients with 152 brain metastases. Clinical and prognostic factors were further analyzed by independent analysis. Kaplan–Meier curves were constructed for overall survival and local control. The median follow-up period was 12 months (range, 1–37 months).

Results: The median age was 61 years (range, 27–85 years) and Karnofsky performance status >70 in 96% of the patients. The median overall survival rate was 15.5 months (95% confidence interval [CI], 10.23–24.3 months). Overall 3-month, 6-month and 1-year local control rates were 98% (95% CI, 85–99%), 96% (95% CI, 82–99%), and 90% (94% IC, 76–96%), respectively. Local failure (LF) was observed in 6 patients (18 lesions). No late complications, such as radiation necrosis, were observed during the follow-up period.

Conclusions: CKRS achieves excellent overall survival and local control rates with low toxicity in patients with brain metastases.

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1. Background

Brain metastases (BMs) are the most common forms of intracranial tumor, occurring in approximately 20–40% of all cancer patients.[1,2] Causing a significant impact on morbidity and mortality with a median survival of untreated patients being 1–3 months.[3] Treatment options for BMs include surgical resection, whole-brain radiation therapy (WBRT) and stereotactic radiosurgery (SRS).[4]

WBRT has been used for decades as a standard therapy for BMs. Currently, its use is debatable, as although greater distant brain control rates are observed, there is no impact on survival and the effect on patient's cognition and quality of life could overweigh potential benefits.[5] Randomized trials have demonstrated improved local control and quality of life when using SRS alone or in combination with WBRT, particularly in those with a single metastasis regardless of recursive partitioning analysis (RPA) and those with RPA Class 1 with up to three metastases.[5–8]

The CyberKnife system has proven to achieve all the goals of radiosurgery by delivering high, ablative radiation dose with maximal dose fall-off outside the treatment volume with a frameless sub-millimeter accuracy. Although CyberKnife Stereotactic Radiosurgery (CKSRS) for brain metastasis is a common practice, few data exist regarding this technique's efficacy, safety, and optimal patient selection.[9–12]

2. Aim

Stereotactic radiosurgery is increasingly employed for the treatment of brain metastases, both as an adjuvant to surgical resection, and as a primary treatment modality. The aim of this study is to evaluate the local control of disease and overall survival in patients with brain metastases treated with CyberKnife Stereotactic Radiosurgery (CKRS) and review the published data.

3. Materials and methods

3.1. *Study design*

Using a retrospective cohort design, we reviewed 49 patients (corresponding to the authors) with brain metastases of any primary tumor treated with stereotactic radiosurgery at the Christus Muguerza Hospital Alta Especialidad from October 2011 to January 2017. Collected data included gender, age, Karnofsky Performance Scale (KPS), primary site of the tumor, recursive partitioning analysis (RPA) class, number and location of brain metastases, previous local treatment (surgery or WBRT), dosimetry, prognostic index of graded prognostic assessment (GPA) and diagnosis-specific GPA.

3.2. *Radiosurgery characteristics*

All treatments were delivered using the CyberKnife Frameless Radiosurgical System (Accuray, Sunny-vale, CA, USA). A high resolution computed tomogram (CT) was obtained followed by a magnetic resonance imaging (MRI) to fused images for target identification. Dose planning was performed with the Multiplan Software (Accuray Inc., Sunyvale, CA, USA). The gross tumor volume (GTV) was delineated as the edge of contrast enhancement and was considered the same as clinical target volume (CTV). The planning target volume (PTV) was defined as CTV plus a 2 mm margin.

The prescription dose and fractionation were decided following the RTOG 90-05 guidelines and the preference of the treating physician according to radio-sensitivity of the primary tumor, tumor volume, tumor location and distance from critical structures. The treatment volumes were prescribed to a medium 86% isodose line (range 78–90%).

3.3. *Follow-up*

Follow-up, including physical evaluation and gadolinium-enhanced MRI, were performed 3 months after SRS and every 3 to 6 months thereafter until the death or the date of closure of the study (January 2017). Follow up information was available for 42 patients. The median follow-up period was 12 months (range, 1–37 months).

3.4. *Statistical methods*

Overall Survival (OS) rate was the primary endpoint, secondary endpoints included Local Control (LC) and Distant Brain Control (DBC). Data analysis was performed using STATA version 14.2 (StataCorp LCC, TX, USA). LC was defined as a stabilization or reduction of the tumor and "contrast enhancement" on MRI, and DBC as the absence of new brain metastases or leptomeningeal disease outside the radiosurgical target volume. Kaplan–Meier rates for OS were calculated from the date of CKSRS to the date of patient's last follow up clinic visit or death. Patients who received salvage treatment with new SRS or WBRT where followed up for survival and toxicity.

Patients were classified according to the GPA and diagnosis-specific GPA. The log-rank test was used for univariate analysis to assess predictive factors associated with OS. Estimated hazard ratios (HRs) were calculated. A P value <0.05 was considered statistically significant. Statistical test was based on a 2-sided significance level. The following clinical factors were investigated for their association with OS: age, gender, Karnofsky, GPA Score, RPA Class, number of metastases, extracranial disease, prior WBRT and tumor volume.

4. Results

4.1. *Patient characteristics*

Forty-nine patients with 152 brain metastases were identified, with a median age of 61 years (range, 27–85 years) and Karnofsky performance status >70 in 96%. The most frequent primary tumor type was the lung cancer (48%) followed by the breast cancer (12%) and melanoma (10%). Patient's characteristics are summarized in Table 1 and diagnosis-specific GPA in Table 2.

Fifteen patients had received prior local treatment including WBRT, surgery or both. Nine patients had received surgery as a primary treatment, of which 5 patients received adjuvant SRS to the resection cavity and 4 patients as salvage therapy