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ORIGINAL ARTICLE

Evaluation of Risk Factors for Radiation Necrosis among Patients Undergoing Cranial Stereotactic Radio surgery

S Mallik

Associate Professor, Department of Radiotherapy, Kasturba Medical College, Manipal, Karnataka, India

ABSTRACT:

Aim: The aim of the study was to evaluate risk Factors for Radiation Necrosis among Patients Undergoing Cranial Stereotactic Radio surgery. **Materials and methods:** This retrospective analysis included 100 patients, with a female predominance (75 cases). The median age of the cohort was 45 years, ranging from 18 to 70 years. The study analyzed patients who underwent stereotactic radio surgery (SRS) for intracranial neoplasms, including brain metastases (BM), meningiomas, and vestibular schwannomas (VS). Clinical, epidemiological, and radiological data, such as tumor size and surrounding edema, were collected from electronic patient records and imaging databases. Statistical analysis was done using SSPS software. **Results:** The distribution of primary tumors includes non-small cell lung carcinoma at 37%, melanoma at 24%, breast carcinoma at 9%, renal cell carcinoma at 12%, cancer of unknown primary at 10%, and other types at 8%.The analysis conducted through Cox regression did not reveal any significant associations with gender, prior SRS treatment or surgical resection, the presence of surrounding edemaor the extent of multiloculartumor growth in relation to the development of radiation necrosis (RN). Furthermore, age was identified as a factor significantly linked to an increased risk of RN. **Conclusion:** Higher radiation doses and larger tumor size are key risk factors for developing radiation necrosis (RN) after cranial stereotactic radiosurgery (SRS).

Keywords: Stereotactic, radio-surgery, necrosis

Corresponding author: S Mallik, Associate Professor, Department of Radiotherapy, Kasturba Medical College, Manipal, Karnataka, India

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INTRODUCTION

Oncologists will be treating a greater absolute number of elderly patients than ever before. In 2000, the sector of the French population that was 65 years and older was 16% and should reach 24% in 2030. Life expectancy in Western countries is increasing. Men living to be 80 can expect to live approximately 7 years longer, and those beyond 85 years can expect to live another 5; women will enjoy an additional 1–2 years of longevity. A healthy 75-year-old has a life expectancy of 11 years.[1- 3]These numbers exceed the average survival durations of most untreated cancers. The elderly are at risk of having their lives shortened by cancer. One can thus assume that successful treatments, given that their toxicities are acceptable, could lead to survival advantages. Cancer is more frequent with increasing age, and in general it is assumed that survival after a cancer diagnosis declines as age increases.[4] Because of the relatively favorable survival of patients with one or two brain metastases, the treatment is frequently more aggressive than for patients with multiple brain metastases. Often, this includes surgery (OP) or stereotactic radiosurgery (SRS) alone or in addition to whole-brain radiotherapy (WBRT).[5- 7]Hence; the aim of the study was to identify risk factors associated with the development of radiation necrosis in patients undergoing cranial stereotactic radiosurgery (SRS).

MATERIALS AND METHODS

This retrospective analysis included 100 patients, with a female predominance (75 cases). The median age of the cohort was 45 years, ranging from 18 to 70 years. The study analyzed patients who underwent stereotactic radiosurgery (SRS) for intracranial neoplasms, including brain metastases (BM), meningiomas, and vestibular schwannomas (VS). Clinical, epidemiological, and radiological data, such as tumor size and surrounding edema, were collected from electronic patient records and imaging databases. SRS was performed using. Post-SRS follow-ups included routine MRI scans at defined intervals, assessing tumor progression and radiation necrosis (RN), which was primarily managed conservatively with steroids and bevacizumab, with surgery reserved for severe cases. Statistical analysis was done using SSPS software.

RESULTS

The distribution of primary tumors includes non-small cell lung carcinoma at 37%, melanoma at 24%, breast carcinoma at 9%, renal cell carcinoma at 12%, cancer of unknown primary at 10%, and other types at 8%.The study analyzedtumor characteristics, treatment history, and outcomes in patients undergoing cranial stereotactic radiosurgery (SRS). The largest mean tumor diameter was 18.1 ± 2.6 mm, with a median radiation dose of 16 Gy. Most patients 23 % had no prior brain radiation, while 11% had

undergone one or more previous treatments. SRS was the primary treatment in 70.2% of cases, while 15.1% had prior surgery. The median follow-up was 24 months, during which radiation necrosis (RN) developed in 12% of patients, with a mean onset of 6 months. Nearly half (45%) of RN cases were symptomatic. Among affected patients, 33% required treatment, primarily with dexamethasone or bevacizumab, while two cases required surgery. Two additional patients, due to poor clinical status, received only supportive care.The hazard ratio (HR) associated with tumor diameter was calculated to be 1.123, and a p-value of 0.000. In contrast, the HR for the dose of stereotactic radiosurgery (SRS) was found to be 1.425, and a p-value of less than 0.002. The analysis conducted through Cox regression did not reveal any significant associations with gender, prior SRS treatment or surgical resection, the presence of surrounding edemaor the extent of multiloculartumor growth in relation to the development of radiation necrosis (RN). Furthermore, age was identified as a factor significantly linked to an increased risk of RN.

Table 1: Primary tumor of BM undergoing radio surgery

Primary	N	Percent of all Tumors
Non small cell lung carcinoma	37	37%
Melanoma	24	24%
Breast Carcinoma	9	9%
Renal Cell Carcinoma	12	12%
Cancer of unknown primary	10	10%
Other	8	8%

Table 2: RN among vestibular schwannoma (VS), brain metastasis and meningioma

Variable	VS	BM	Meningioma
Mean diameter (mm)	16.2	15.9	18.2
RN	2	8	6
Median SRS dose (Gy)	14	19	15
RN months median (months)	11	10	9

DISCUSSION

Cancer can manifest at any age, yet its prevalence tends to escalate with advancing age. A comparative study conducted across seven industrialized nations revealed that in 2000, the percentage of individuals aged 65 years and older varied between 12.6% and 18.1%. Projections indicate that by 2030, this demographic may constitute approximately 20% to 28% of the total population. Additionally, individuals in average health who reach the age of 75 can now anticipate an average additional lifespan of 11 years, while a healthy 85-year-old has a median life expectancy of 6 years. The incidence of brain metastases varies significantly, ranging from 5% to 40% among patients with systemic cancer, depending on factors such as the specific type of cancer, the stage at which it is diagnosed, and various tumor- and treatment-related variables. There has been a notable increase in the incidence of brain metastases, attributed to several factors, including enhanced survival rates in patients with localized cancers due to earlier detection, improved imaging techniques that allow for better identification of metastatic disease, and innovative treatment approaches, many of which do not effectively penetrate the blood-brain barrier. While further research is necessary to fully comprehend the biology and epidemiology of brain metastases associated with solid epithelial cancers, recent prospective studies have indicated a survival benefit from surgical intervention and whole brain radiation therapy (WBRT), or a combination of WBRT and stereotactic radiosurgery (SRS) for treating brain metastases. However, these studies, along with some retrospective analyses, highlight the significant negative impact of age on prognosis, particularly in patients aged 65 years and older. To date, there has been a lack of comprehensive investigation into the effectiveness of SRS, either as a standalone treatment or as part of a multidisciplinary strategy for managing brain metastases in elderly patients, specifically those aged 75 years and above at the time of diagnosis.[6- 9]

The distribution of primary tumors includes non-small cell lung carcinoma at 37%, melanoma at 24%, breast carcinoma at 9%, renal cell carcinoma at 12%, cancer of unknown primary at 10%, and other types at 8%.The study analyzedtumor characteristics, treatment history, and outcomes in patients undergoing cranial stereotactic radiosurgery (SRS). The largest mean tumor diameter was 18.1 ± 2.6 mm, with a median radiation dose of 16 Gy. Most patients 23 % had no prior brain radiation, while 11% had undergone one or more previous treatments. SRS was the primary treatment in 70.2% of cases, while 15.1% had prior surgery. The median follow-up was 24 months, during which radiation necrosis (RN) developed in 12% of patients, with a mean onset of 6 months. Nearly half (45%) of RN cases were symptomatic. Among affected patients, 33% required treatment, primarily with dexamethasone or bevacizumab, while two cases required surgery. Two additional patients, due to poor clinical status, received only supportive care.The hazard ratio (HR) associated with tumor diameter was calculated to be

1.123, and a p-value of 0.000. In contrast, the HR for the dose of stereotactic radiosurgery (SRS) was found to be 1.425, and a p-value of less than 0.002. The analysis conducted through Cox regression did not reveal any significant associations with gender, prior SRS treatment or surgical resection, the presence of surrounding edemaor the extent of multiloculartumor growth in relation to the development of radiation necrosis (RN). Furthermore, age was identified as a factor significantly linked to an increased risk of RN.Kim SHet al evaluated the therapeutic effect of stereotactic radiosurgery (SRS) in patients aged > or =75 years who presented with brain metastasis. The authors analyzed the data from 44 consecutive patients treated with SRS for > or =1 brain metastasis. The median age at the time of treatment for brain metastases was 79.3 years (range, 75 years-86 years), and the median Karnofsky performance status was 80 (range, 50-100). At the time of SRS, 31 patients were treated for a single metastasis, and the remaining 13 patients were treated for > or =2 lesions (n = 74 lesions). The median tumor volume was 1.2 cm(3) (range, 0.007 cm(3)-22.5 cm(3)). The median maximal and marginal doses were 36 grays (Gy) (range, 18.8 Gy-48.2 Gy) and 20 Gy (range, 10 Gy-24 Gy), respectively. Median survival was 7.3 +/- 1.65 months (range, 1.6 months-38.9 months) from the time of diagnosis of brain metastasis. Median survival of the patients with a single brain metastasis (10.1 +/- 1.92 months) was longer than that of the patients with > or =2 metastases (6.6 +/- 1.28 months) (P <.02). A single lesion was found to be an independent favorable prognostic factor (P +/- = +/- .017; odds ratio, 2.385 [95% confidence interval, 1.167-4.874]) in univariate and multivariate analysis. Patients with nonsmall cell lung cancer fared worse than patients with other tumor types (survival of 6.5 +/- 0.70 months vs 10.1 +/- 2.33 months [P<.05]). SRS for patients aged > or =75 years with brain metastases is an effective and safe treatment modality that appears to improve survival, with outcomes that compare favorably with those reported for younger patients in an appropriately selected population.[10]Noel G et alevaluated the outcomes of radiosurgery for brain metastases in patients 65 years or older. 117 patients (47 women, 70 men), median age 71 years (range, 65-86 years), received radiosurgery for 227 metastases. Sixty-one patients (55%) presented symptoms in relation to the brain metastases. Thirty-eight patients (32%) received whole-brain radiotherapy. Median metastasis diameter and volume were 21 mm (range, 0.5-75 mm) and 1.7 cc (range, 0.02-71 cc), respectively. Median follow-up was 7 months (range, 1-45 months), 9.5 months for alive patients (range, 1-45 months). Median minimum and maximum doses were 14.5 Gy (6.5 Gy, 19.5 Gy), and 20.4 Gy (13.2 Gy, 41.9 Gy), respectively. Median survival was 8 months from the date of radiosurgery. Overall survival rates at 6 and 24 months were 58% +/- 5% and 13% +/- 4%, respectively. According to multivariate analysis, a low Karnofsky performance status was an independent unfavorable prognostic factor for overall survival (p = 0.003; odds ratio [OR] = 0.28; 95% confidence interval [CI], 0.14-0.56). Median brain disease-free survival was 10 months. Brain disease-free survival rates at 6 and 24 months were 67% +/- 6% and 40% +/- 7%, respectively. According to multivariate analysis, a radiosensitive lesion was an independent favorable factor (p = 0.038; OR = 0.42; 95% CI, 0.18-0.95); more than two metastases and a low Karnofsky performance status were independent unfavorable factors for brain disease-free survival (p = 0.046; OR = 2.15; 95% CI, 1.01-4.58 and p = 0.003; OR = 30.4; 95% CI, 3.1-296, respectively). Local control rates were 98% +/- 2% and 91% +/- 8.5% at 6 and 24 months. Out of the 61 patients presenting symptoms before radiosurgery, complete symptomatic response was achieved in 12 patients (20%), partial improvement in 25 (41%), stabilization in 7 (11%), and worsening in 4 (6%) related to a progression of the irradiated metastasis. Seven cases of radionecrosis were described and were related to the margin dose (p = 0.03).Radiosurgery for elderly patients was effective and safe.[11]

CONCLUSION

Our study highlights that higher radiation doses and larger tumor size are key risk factors for developing radiation necrosis (RN) after cranial stereotactic radiosurgery (SRS).

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