Stereotactic Radiosurgery of Colorectal Carcinoma Brain Metastasis: A Multi-Institutional Experience.

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Abstract

Purpose: Colorectal cancer is one of the most common cancers with one of the poorest survival rates following brain metastasis. Only a few studies have described outcomes after radiosurgery and predictors of mortality in these patients. We describe a multi-center experience in the treatment of colorectal cancer metastases to the brain using stereotactic radiosurgery.

Material and Methods: A retrospective review of 66 patients treated over 1993 to 2009 with at least one follow-up was undertaken. Median time to death and its predictors were calculated using Kaplan Meier survival analysis and Cox proportional hazard model.

Results: Overall median survival for patients with colorectal cancer was 4.05 months with a mortality of 58 (84.06%) patients over a mean follow-up of 7.03+12.44 months. Both survival analysis and multivariate analysis revealed KPS>70 as the only significant predictor of survival (median survival KPS >70: 6.91 months versus KPS < 70: 1.74 months, p=0.004; Hazard ratio for KPS>70 was 0.31, p=0.001). When total volume did not exceed 5.4 cc^3, the patients with volume distributed over fewer lesions had improved survival. No such association was observed with higher volumes.

Conclusions: SRS moderately improves survival of patients with colorectal cancer metastatic to brain. Higher KPS predicts favorable prognosis in these patients.

Categories: Radiation Oncology, General Surgery, Neurosurgery
Keywords: brain metastasis, colorectal cancer, stereotactic radiosurgery, Volume distribution

Introduction

Colorectal cancer is the fourth most common form of cancer constituting 9.4% of all cancers in men and 10.1% of cancers diagnosed in women worldwide [1]. Despite such frequent occurrence of colorectal cancer, metastatic lesions to the brain are rare and occur in only 0.64-6% of patients. In comparison, other common cancers like non-small cell lung cancer and breast cancer have rates of 50% and 12% developing brain metastasis, respectively [2-5]. Although lung and liver are the most frequent sites of metastases from colorectal carcinoma with increasing survival, distant lesions, such as the brain, are becoming more frequent [6-8].

Although surgical resection with postoperative radiotherapy has been the standard of care in the management of cerebral metastases [9-11], stereotactic radiosurgery provides an alternative treatment that spares the surrounding parenchyma, has less treatment related morbidity than surgery [12], and can access lesions that are inoperable. Radiosurgery in well-selected patients enhances survival from 2.1 - 3 months in those who receive palliative treatment using steroids or whole brain radiation therapy [13-15] to 7.1 - 11 months. Unfortunately, most existing studies are based on heterogeneous histological groups or pertain to the primaries most likely to metastasize to brain, like non-small cell lung carcinoma [16-18], breast carcinoma [19-21], melanoma [22] or renal cell carcinomas [23-24]. Only three studies, to our knowledge, have reported outcomes of radiosurgical treatment of brain metastasis from colorectal primaries - a condition that is becoming increasingly common [3, 25-26]. The challenge in grouping colorectal cancer patients with other tumor types that more commonly spread to the brain is the difficulty in accounting for extracranial disease burden. For example, colorectal adenocarcinoma frequently spreads to the liver and lungs, sites that are not as commonly seen in other tumor types. Therefore, systemic disease burden is often a confounding factor when studying patients with colorectal metastases to the brain. Therefore, extrapolating radiosurgery data derived from other tumor types is sub-optimal when treating patients with intracranial colorectal cancer metastases [10, 25]. We describe outcomes of radiosurgical treatment of brain metastasis from colorectal carcinoma at two tertiary care centers.

Materials And Methods

Patients and methods

We retrospectively reviewed data collected from 69 patients who received stereotactic radiosurgery to treat metastatic brain lesions originating from colorectal carcinoma. After excluding three patients who did not return to follow-up after radiosurgery, outcome regarding tumor progression and survival were available for 66 patients. Amongst these patients, 51 patients were treated at Miami Neuroscience center, Miami, FL (MNC) from 1993 to 2009, while 15 patients were treated at Johns Hopkins Hospital, Baltimore, MD (JHH) between 2003 and 2007. Approval was gained from the Institutional Review Board at JHH for chart review with waiver of consent and use of data from the MNC. The histopathological diagnosis was confirmed by biopsy of the tumor at primary site or from biopsy of a metastatic lesion at an extracranial site or from specimen obtained during craniotomy. According to our treatment protocol, neurological and radiological progression of metastatic disease was monitored with a follow-up initially at four weeks post-radiosurgery and subsequently at intervals of three months. Any local recurrence or appearance of new lesions was treated with either a subsequent session of radiosurgery or craniotomy.

Gamma Knife

All lesions were treated using a Leksell Gamma Knife model U, model B or model C (Elekta Instruments, Stockholm, Sweden). The recommendation for Gamma Knife therapy and the treatment plan were determined after consultation with a neurosurgeon and a radiation oncologist at the respective centers. Patients harboring multiple lesions were sometimes treated in multiple sessions. The prescription dose was based upon volume, number and location of lesions, with deep lesions and those located in proximity to critical neurovascular lesions receiving lower dose. The mean prescription dose at MNC was 16.93+2.66Gy, whereas patients at MTH received a similar dose with a median of 17.66+1.44Gy (p-0.31).

Statistical analysis

The demographic and clinical features of patients included in this study were summarized and compared between Mil and MNC. Frequencies and percentage were obtained when data was categorical and compared between two centers using Fisher's Exact test. Similarly, measures of variables continuous in nature were summarized as median and interquartile range (IQR) and compared using Wilcoxon Rank-Sum test. When treatment was administered in multiple sessions, we recorded as the treatment dose, the lowest dose received by lesions at all sessions. Survival times were calculated as time to mortality from the first radiosurgical treatment and also from initial diagnosis of brain metastasis. The progression-free survival (PFS) was calculated as time since treatment until subsequent intracranial progression or death. The median survival times and progression free survival were calculated using Kaplan Meier Analysis. Cumulative failure rates were derived from life table analysis. Patients were censored at last follow-up when there was no mortality or progression during Kaplan Meier analysis for survival and PFS, respectively. The median survival and PFS times were further stratified by the clinical and demographic features, such as treatment centers (JM and MNC), age groups (age < 65 years, age >65 years), Kamofsky performance scores (KPS) (KPS >80, < 70), number of lesions (solitary lesion, two to three lesions, >3 lesions),volume (by quartiles) and interval between diagnosis of primary cancer to diagnosis of intracranial metastasis (<2 year, >2 year). The survival times were compared between the strata and the two centers using Log Rank Test. Cox proportional hazard model was used to estimate relative risk of mortality attributable to covariates described initially using univariate analysis. We did not stratify our analysis by treatment center due to the small number of patients at each center. A stepwise backward selection of variables was undertaken for multivariate analysis. Cumulative incidence of brain metastases related (BMR) mortality was derived using non-brain metastases related (non-I3MR) mortality as competing risk factor and compared between covariates using Grays test.

All p-values reported are two-sided. The analysis was performed using Stata version 12 (Stata Corp LP: College Station, TX) and R version 2.13.0 (2011-04-13).

Results

The clinical and demographic characteristics of the patients at two centers have been summarized in Table *1*. Mean age of patients in this series was 65.10+11.91 years. Median KPS of the patient population was 80 with 72% patients having KPS >70. The majority of patients in this series had colon cancer (64 (92.75%) patients), while rectal carcinoma was present in 5 (7.25%) patients. Median time to development of brain metastasis from diagnosis of the primary cancer was 31.95 months (IQR: 15.03- 50.93 months). Three patients had synchronous brain metastasis at the time of diagnosis of colorectal cancer; follow-up was available for two of these patients: one patient died at 1.45 and the other at 4.31 months after radiosurgical treatment.

	MNC	JHH	p
N	54	15	
Age			
Age	66.5 + 11.83	60.0 + 12	0.06
Age > 65	32 (59.26)	5 (33.33)	0.08
Age < 65	22 (40.74)	10 (66.67)	
Gender			
Males	30 (55.56)	11 (73.33)	0.17
Female	24 (44.44)	4 (26.67)	
Number of lesions			
1 lesions	28 (51.85)	10 (66.67)	
2-3 lesions	18 (33.33)	3 (20.0)	0.61
> 3 lesions	8 (14.81)	2 (13.33)	
Lesion volume			
< 5.6ml (p25)	9 (16.67)	10 (66.67)	
5.6-11.4ml (p25-p50)	12 (24.07)	3 (20)	0.002
11.4-17.3ml (p50-p75)	16 (29.63)	1 (6.67)	
> 17.3ml (>p75)	16 (29.63)	2 (13.33)	
KPS			
Median KPS (IQR)	80 (70-90)	90 (80-100)	0.11
KPS ≤ 70	13 (32.50)	1 (10)	0.35
KPS > 70	41 (67.50)	9 (90)	
Time to diagnosis of metastasis			
≤ 12 months	7 (15.56)	1 (6.67)	0.35
> 12 months	38 (84.44)	14 (93.33)	
Treatment			
GK	46 (88.46)	13 (86.67)	0.57
GK+WBRT	6 (11.54)	2 (13.33)	
Median treatment dose (Gy)	17 (16-18)	18 (16-18)	0.31

TABLE 1: Demographics and Clinical Features of Patients

At least one follow-up visit was available for 66 patients, who were included in the study. Fifty-eight (84.06%) patients died over a mean follow-up of 7.03+12.08 months after radiosurgery. Median survival from time of radiosurgery was 4.05 months (95% CI: 2.40-5.36 months) and from the time of diagnosis of brain metastasis was 6.67 months (95% CI: 5.06-10.52 months) observed during the study period. A comparable survival (p-0.21) was observed at two centers - 3.91 (95% CI: 2.2-4.86 months) at MNC and 7.07 (95% CI: 1.67-15.36 months) at Hifi. Survival at six months and one year was 34.77% (95% CI: 23.18-46.62%) and 14.64% (95% CI: 6.95-25.04%). Data regarding cause of death was available for 45 patients, of whom three (6.67%) had brain metastasis related mortality and 42 (93.33%) patients died from extracranial disease progression. Three patients who died from brain metastasis related causes survived for 1.88, 2.43 and 18.42 months since radiosurgery.

Data regarding KPS scores at time of Gamma Knife were available for 47 patients. Amongst 33 patients with KPS > 70, median survival was 6.91 months, and 27 (81.8%) patients died in the time period captured by this study. Median survival in 14 patients with KPS <70 was 1.74 months (p-0.004) with 100% mortality during follow-up (Figure *1*). There was no significant difference in survival by factors, such as number of lesions, total volume of lesion, or age of the patient (Table *2*, Figures *1-4*).
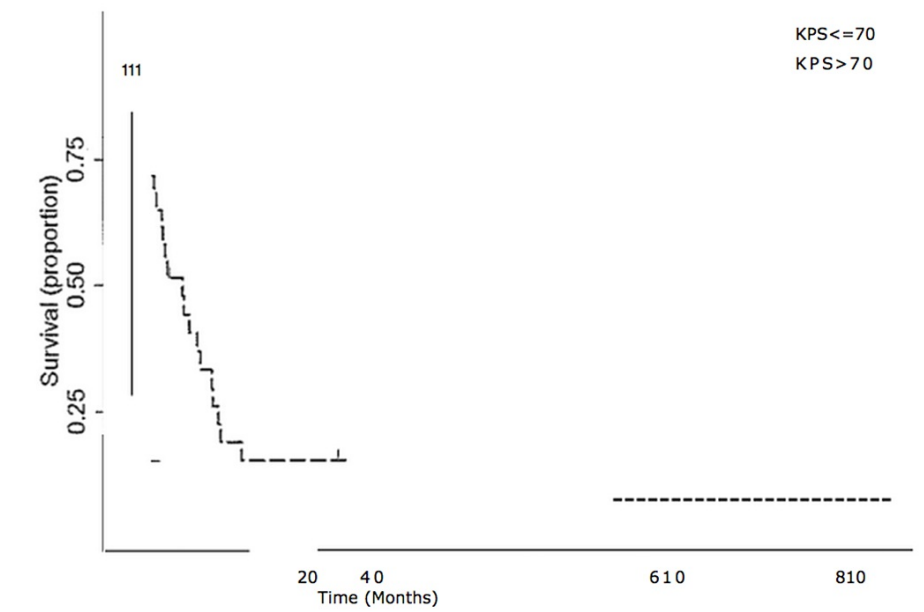

FIGURE 1: Survival by KPS

Strata	N	Dead (%)	Median Survival (months)	Log-rank p-value (between strata)
Center				
MNC	51	48 (94.11)	3.91 (2.2 - 4.84)	0.21
Hopkins	15	10 (66.67)	7.07 (1.6 - 15.36)	
Age				
Age < 65	29	23 (83.18)	4.77 (2.36 - 6.91)	0.87
Age ≥ 65	37	35 (89.74)	4.05 (2.04 - 7.07)	
Gender				
Females	27	23 (83.18)	4.11 (2.43 - 6.91)	0.87
Male	39	35 (89.74)	4.05 (2.00 - 7.07)	
Number of lesions				
1 lesions	35	29 (82.85)	3.95 (2.04 - 7.08)	0.81
2-3 lesions	21	19 (90.4)	3.16 (1.58 - 5.43)	
>3 lesions	10	10 (100)	5.1 (1.78 - 9.93)	
Lesion volume				
<5.6ml (p25)	19	15 (78.94)	6.91 (1.48 - 9.93)	0.33
5.6 - 11.4ml (p25-p50)	15	14 (93.33)	3.03 (1.88 - 7.07)	
11.4 - 17.3ml (p50-p75)	15	14 (93.33)	4.74 (2.2 - 4.9)	
>17.3ml (>p75)	17	15 (88.23)	3.16 (1.51 - 7.6)	

Distribution of volume				
Solitary small lesion (volume <5.6cc)	9	6 (66.7)	8.48 (0.95 - .)	0.037
2-3 lesions with total volume <5.6cc	6	5 (83.33)	1.48 (0.85 - .)	
>3 lesions with total volume<5.6cc	4	4 (100)	5.36 (1.78 - .)	
Solitary large lesion (volume >5.6cc)	26	23 (88.46)	2.43 (2.04 - 4.9)	0.62
2-3 lesions with total volume >5.6cc	15	14 (93.33)	4.31 (1.88 - 10.1)	
>3 lesions with total volume >5.6cc	6	6 (100)	4.84 (1.91 - .)	
KPS				
KPS ≤ 70	14	14 (100)	1.74 (1.12 - 2.43)	0.0004
KPS > 70	33	27 (88.18)	4.11 (2.2 - 7.6)	
Time to diagnosis of metastasis				
≤ 12 months	6	6 (100)	3.95 (1.45 - .)	0.24
>12 months	51	43 (84.33)	4.11 (2.2 - 7.6)	
Treatment				
GK	57	51 (89.47)	4.05 (2.65 - 5.43)	0.75
GK + WBRT	8	6 (75)	4.31 (1.12 - .)	
Dose				
> 18Gy	43	39 (90.69)	2.8 (1.88 - 4.11)	0.66
≤ 18Gy	23	19 (82.60)	9.21 (4.05 - 10.63)	

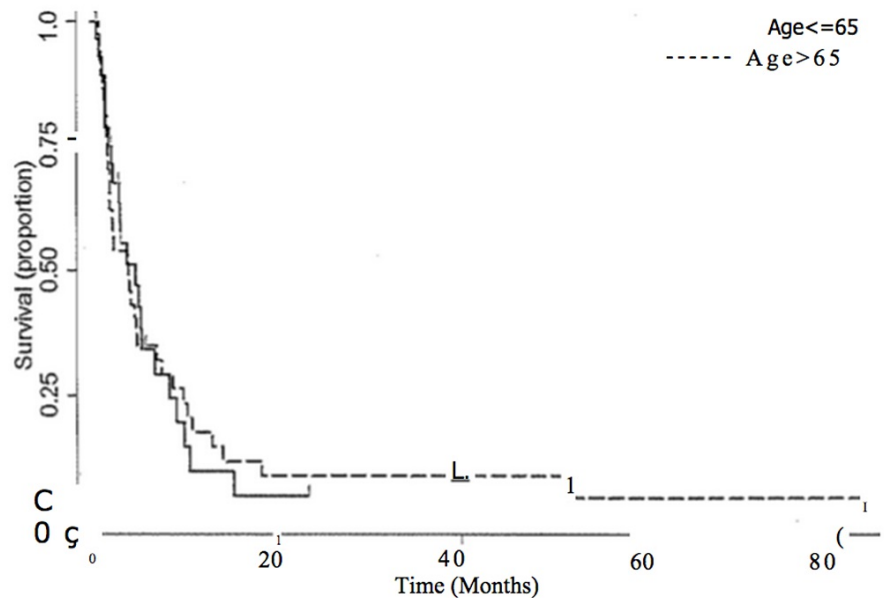**TABLE 2: Survival Time from Gamma Knife Procedure**
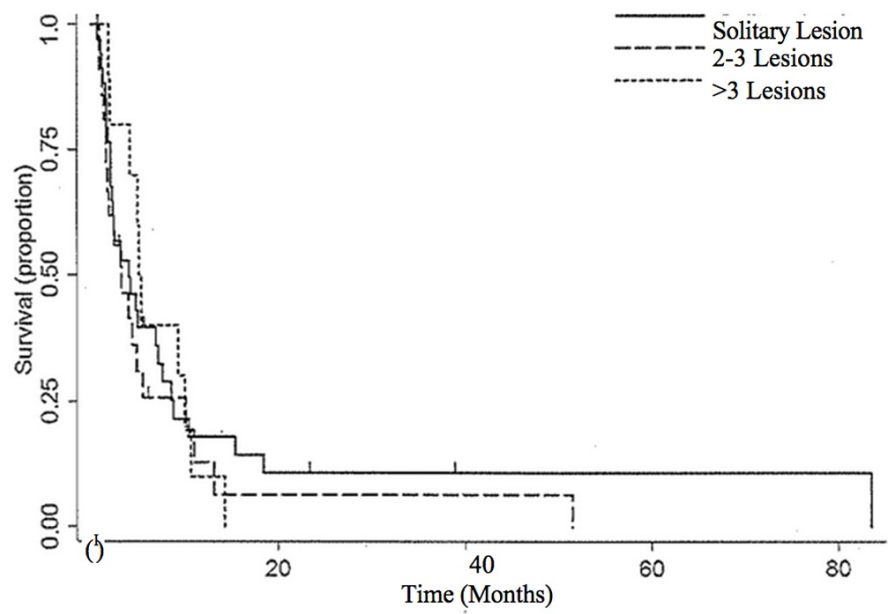

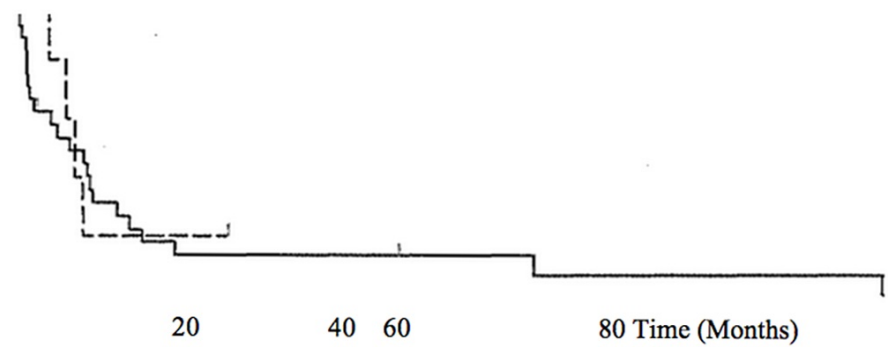**FIGURE 2: Survival by Age**

FIGURE 3: Survival by Lesion Number

FIGURE 4: Survival by Total Volume

Prognostic factor	Odds Ratio (95% CI)	P
Age ≥ 65	0.95 (0.55-1.63)	0.87
KPS ≤ 70	3.22(1.62-6.39)	0.001
Lesions >3	0.90(0.45-1.73)	0.77
Volume >8.4cc	1.45(0.82-2.56)	0.19
Synchronicity of brain metastasis	1.66(0.69-4.01)	0.25
Dose <18	2.69(1.49-4.84)	0.001
Male	1.05(0.62-1.80)	0.21
GK+WBRT	1.14(0.48-2.72)	0.75

TABLE 3: Univariate Hazard Ratios

When evaluating treatment related factors, higher dose of radiation was associated with better survival (Figure 5). Patients who were treated with a dose less than 18 Gy survived for a median of 2.8 months (N:=43, mortality: 90.69%) as compared to 9.21 months in patients (N=23, mortality: 82.60%) who were treated with a dose of 18 Gy or more (p=0.0012). Furthermore, patients who received a repeat Gamma Knife treatment for recurrence of metastatic lesions survived for significantly longer duration (survival: 10.36 months; mortality: 92.85%) than patients who did not receive the subsequent procedure (survival: 3.03 months; mortality: 86.53%), p=0.0079.
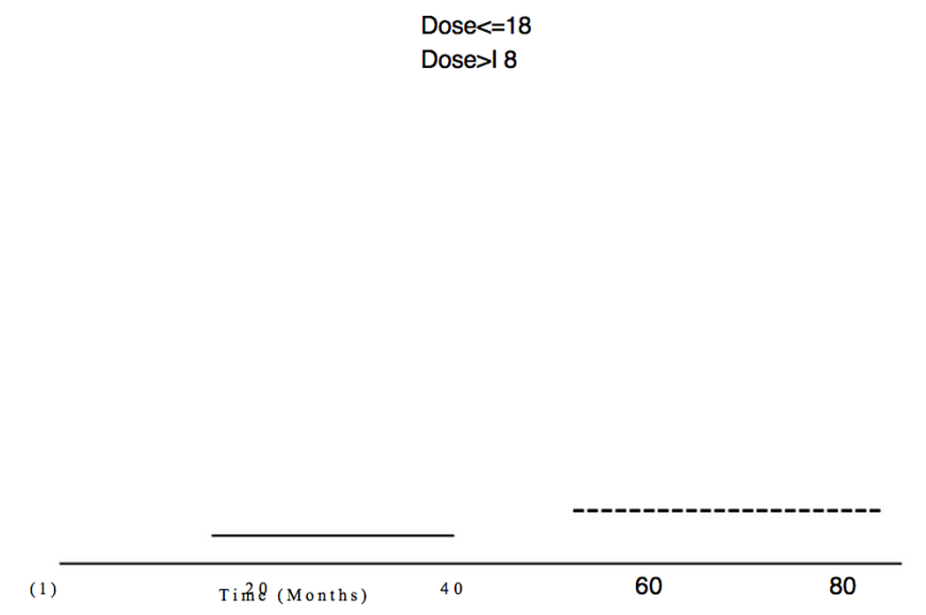

FIGURE 5: Survival by Dose

Cumulative incidence of mortality caused by brain metastases and other causes

Cumulative incidence of brain metastasis related (BMR) and non-BMR mortality using competing risk analysis at 12 months was 4.32% (95%CI: 0.7 - 13.19%) and 84.16 % (95%CI 68.72-92.36%), respectively. While, at 24 months, cumulative incidence of BMR and non-BMR mortality was 6.63% (95%0: 1.5-17.32%) and 88.76 % (95%CI 73.76 -95.43%), respectively.

On univariate analysis, KPS<70 and no repeat treatment, despite recurrence, were found to be significant

predictors of mortality. No other variables, including number of lesions, volume of lesions, adjuvant radiotherapy, age, treatment center, diagnosis of intracranial metastasis within two years of diagnosis of primary colorectal cancers or dose was found to be significant predictor of mortality. Furthermore, when all of these variables were included in a multivariate analysis, only KPS>70 was an independent predictor of survival with patients having KPS>70 being 69% less likely to die. However, when only variables with p value <0.1 were included in multivariate analysis, both KPS>70 and repeat radiosurgery for recurrence were found to be independent predictors of survival. This was so due to greater number of patients with complete data for these two variables when compared to all the variables included in the initial model. On this multivariate analysis, patients with KPS>70 were 27.31% less likely to die than patients with lower KPS (Hazard Ratio: 0.2731, 95% CI: 0.13 -0.56, p=0.001). Also, patients who had subsequent radiosurgery for local recurrence or relapse of intracranial metastasis were 36% less likely to die than patients not treated (Hazard Ratio: 0.3619, 95%0: 0.15-0.82, p= 0.016).

Intracranial progression-free survival

Median intracranial progression free survival (PFS) was 3.03 months in this series with 20.1% patients diagnosed with progression prior to mortality. Progression was treated with a repeat session of radiosurgery. The median PFS in patients with KPS < 70 was 1.74 months as compared to 6.91 months in patients with higher KPS (p=0.004). Importantly, the PFS did not differ by number of lesions or the total volume of lesions.

Discussion

This series describes radiosurgical outcomes of patients with colorectal carcinoma metastases to the brain. An overall median survival of 4.05 months was observed from the time of radiosurgery and 6.67 months after diagnosis of brain metastasis. This contrasts with patients harboring brain metastasis from breast cancer where a median survival of 11-13 months from radiosurgery has been reported [15, 19, 20, 27]. Similarly, higher survival [11-13] is also observed after radiosurgery in lung cancer patients with brain metastases [I5-16]. Our results are in concordance with the three existing series studying colorectal cancer, which report survival ranging from 5-6.7 months after radiosurgery [3,25-26].

Extracranial control, Karnofsky performance, status and age

Variables, such as control of the primary lesion, age and KPS, have been widely studied in the radiosurgery literature [14-16, 20, 24,28-29] and these form the key components of the commonly used RPA scales [13,30]. In this study, Karnofsky performance score (KPS)>70 was associated with higher survival on both univariate and multivariate analysis. Several studies have found the association of KPS>70 with a favorable survival in colorectal carcinoma [3,14,25] as well as other histologies [13,15-17,20,27-29]. In the current study, patients with KPS<70 had a median survival of 1.74 months when compared to 6.91 months in patients who had a higher KPS scores. This finding corroborates the practice that patients with KPS < 70 should be offered palliative treatment with steroids or whole brain radiation, since radiosurgical or surgical intervention does not improve survival.

Patients with metastases to the brain from colon cancer are rarely free of extracranial disease [26]. As a result, some groups have found that increasing extracranial disease burden is associated with mortality in patients with metastatic colorectal cancer to the brain [3,10,14,25-26]. It is thought that extracranial dissemination of colorectal cancer often precedes metastasis to the brain. This could be a result of hematogenous spread of colorectal cancer to the liver via portal drainage. Liver metastases are frequent, occurring in up to 79% of colon cancer patients and carries a poor prognosis [10, 31]. However, in this study, systemic tumor burden was not associated with survival. Although much of the existing opinion and literature considers extracranial control of primary disease to be critical for survival, a few surgical and radiosurgical series of colorectal carcinoma have not found a strong role for systemic disease burden on survival.

In a large surgical series of 100 patients reported by Hammoud, et al., the presence of liver or lung metastatic lesions from colorectal carcinoma was associated with poor survival only on univariate analysis, but this association did hold on multivariate analysis. Surgical resection of brain metastasis was the only significant variable that impacted survival with median survival of nine months in those who underwent surgical resection of lesions as compared to three months in radiotherapy treated patients. Similar to surgical series, some radiosurgical series fail to show statistically proven association of survival and long-term remission with extracranial control. Hasegawa, et al., reported an incidence of 30.8% lung metastasis and 17.9% liver metastasis [25]. Patients with liver metastasis survived for four months as compared to eight months in those without liver metastasis, but this trend did not attain statistical significance (p=0.50). Additionally, patients with well-controlled systemic tumor burden likely have widespread micrometastatic disease that is difficult to pulmonary metastasis survived for a median of eight months as compared to five months in those with no lung lesions, and this too was not statistically significant (p=0.65). However, in view of these trends and other existing literature, they attributed poor survival in patients with colorectal cancer to uncontrolled extracranial metastasis, particularly to the liver [25]. Similarly, in a series reported by De Silva, et al., higher survival was associated with absence of extracranial lesions (7.3 versus 5.1 months) but like others described above, this association did not reach statistical significance (p=0.86). Scoeggl and colleagues also reported a median of 3.5 months survival when extracranial dissemination of colorectal

cancer was present as compared to 5.9 months when extracranial disease was controlled (p=0.25). One potential reason for the lack of association is that even those patients who appear to have well-controlled systemic tumor burden likely have widespread micrometastatic disease that is difficult to detect but impacts survival. Though our series is the largest in the radiosurgical literature reported thus far, it does not investigate the role of extracranial control in management of colorectal cancer brain metastasis due to lack of these data.

Tumor volume and lesion number:

In this series, no significant association was found between the number of lesions or tumor volume and the median time to mortality (Figures 6, 7). Patients with solitary metastasis survived for a median of 3.95 months (95% CI: 2.04-7.07 months) as compared to 4.31 months (95% CI: 1.91-5.43 months) in patients with more than one lesion (p=0-0.77). Univariate Cox regression also failed to find the number of lesions as a predictor of survival. We arbitrarily classified the lowest quartiles of volume (<=5.6cc) as small lesions and explored the influence of distribution of total volume on survival. Patients with small lesions in this series survived for a median of 6.91 months (95%CI 1.48- 9.93 months), while those with larger lesions survived for 3.95 (95%CI 2.36-4.84), (p=0.298). While our results are largely in agreement with other radiosurgery series for colorectal carcinoma brain metastasis that did not find volume or number of lesions to predict survival [3,25-26], in our series, solitary lesions less than 5.6 cc in volume had a significantly higher survival (N=9, median survival: 8.48 months, 95% CI: 0.95-.mortality 67%) than patients with greater volume or multiple lesions (N= 57, Median survival: 3.91 months, 95% CI: 3.03-5.43 months, mortality: 91.22%) P=0.025.

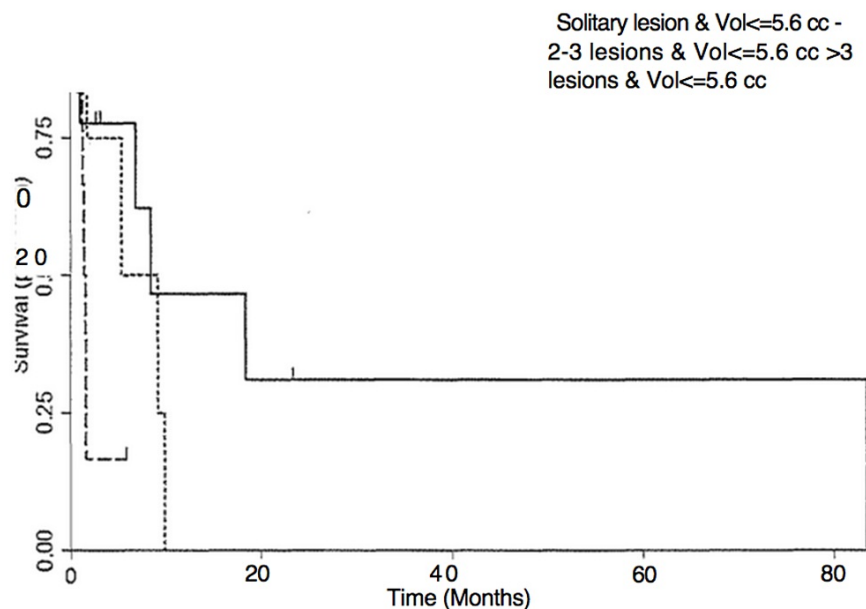**FIGURE 6: Survival by Lesion Number and Volume <5.6 cc**

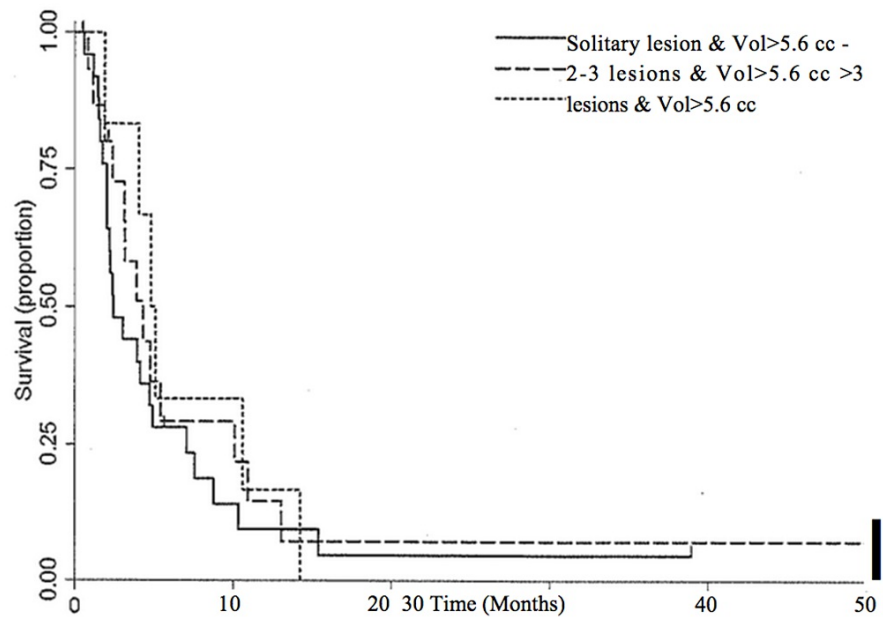**FIGURE 7: Survival by Lesion Number and Volume >5.6 cc**

Furthermore, when total volume did not exceed 5.6 cc, we found significantly lower survival with increasing number of lesions; however, this association was not true for higher total lesion volume. (This interaction of volume and lesion numbers did not stand after multivariate analysis, possibly due to lack of power). This compares favorably with other histological studies whose results suggest patients with solitary or at least fewer than three lesions or smaller total tumor volume have longer overall and progression free survival [29,32-33]. Similarly, Diluna, et al. reported higher survival in patients with fewer than four lesions and total volume less than 5cc [34]. Other series have proposed intracranial location to be possible determinants of mortality, although no statistical association was established [10]. However, elucidating the role of volume and number of lesions in determining mortality, particularly in the context of lesions in deep or eloquent sites, is challenging since colorectal carcinoma brain metastases are infrequent and most studies include small samples size. Given the limited available data, it is unclear whether colon cancer constitutes a unique histological class where survival is not linked to number or volume of intracranial lesions or if those factors do play a key role in determining outcome. As a result, further well-controlled prospective studies are needed to determine if the guidelines used for other histologies apply to this subgroup of patients.

Adjuvant radiotherapy

This series (Figure 8) found no additional survival benefit for patients who received adjuvant whole brain radiotherapy. Survival in the radiosurgery only group was 4.05 months versus 4.31 months in the adjuvant radiotherapy group (v0.75). Furthermore, progression free survival (PFS) did not increase in patients who received adjuvant radiotherapy (median PFS 3.03 months) as compared to those who received only radiosurgery (median PFS 3.03 months) (p=0.57). Other series have similarly found no improvement in overall survival or progression free survival [3,14,25]. Sperduto and colleagues, in a multi-institutional study, found a median survival 7.13 months with adjuvant radiotherapy as compared to 7.33 months with radiosurgery alone (p=0.45). Likewise, Da Silva, et al. reported 6.9 months of median survival with adjuvant radiotherapy, whereas patients who received only radiosurgery survived for a median of 6.6 months (p=0.93). A team led by Hasegawa reported a median survival of nine months with adjuvant radiotherapy as compared to five months without (p=0.81) [25]. However, in this series, prior surgery was correlated with better survival (11 months versus five months, p-0.047) [25]. Similar to this Hammoud, et al. reported decline in risk of mortality by 87% and 88%, respectively, in groups treated with surgical resection (p<0.001) and surgery with adjuvant radiotherapy (p<0.001) as compared to conservative management. Our series did not address the role of surgery due to lack of relevant data.
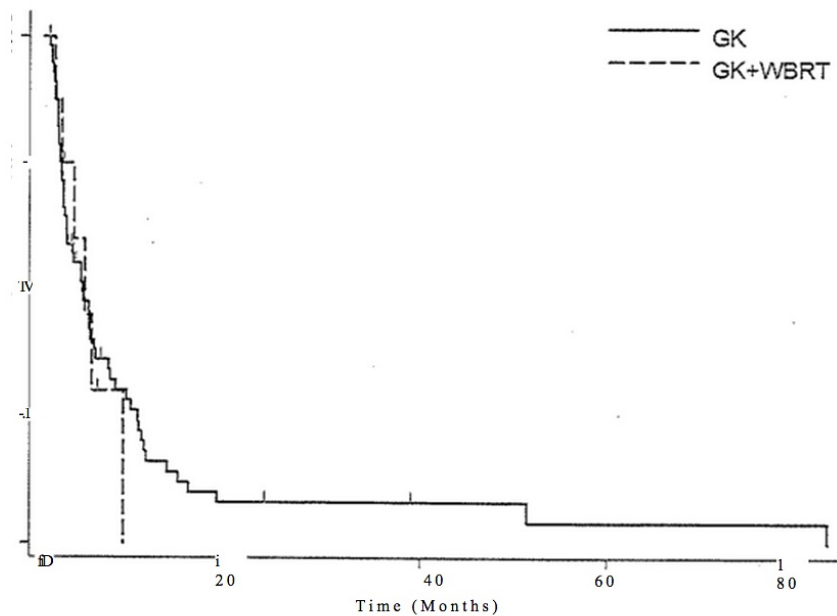
FIGURE 8: Survival by Adjuvant

Multiple procedures for recurrence:

In this study, patients who received additional treatments for progression had a greater survival than patients who received radiosurgery for only the initial metastatic lesions (median survival: 10.36 months 95% CI: 4.77 - 14.24 months versus median survival: 3.03 months, 95%CI 1.91-4.31 months p=0.0079). On univariate analysis, patients who received additional procedures were 59% less likely to die when compared to those with only a single procedure (Hazard ration: 0.411; 95% CI 0.209-0.807, p-0.010). Multivariate analysis revealed administration of additional Gamma Knife sessions to be an independent predictor of survival (Hazard ratio: 0.361, 95% CI: 0.157-0.829, p-0.016). In this series, 14 (20.29%) patients underwent repeat radiosurgery for recurrence and may represent a subgroup of patients with relatively less aggressive cancer or may have different patterns of systemic spread, thereby confounding the results.

Conclusions

Colorectal cancer metastatic to the brain carries with it a poor prognosis. A moderate improvement in survival after radiosurgery is seen only in the subgroup of patients with KPS>70. Larger prospective studies are needed to identify ideal candidates for aggressive management.

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study. The Institutional Review Board at Johns Hopkins Hospital issued approval N/A. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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