IS PALLIATIVE RADIOTHERAPY SAFE IN LARGE HEPATIC LESIONS?

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Schulich MEDICINE & DENTISTRY

Introduction

The size of hepatic lesions is associated with a poor prognosis and limits treatment options. Radiation therapy (RT) may be an option, but larger radiation fields may result in increased toxicity and these patients may be underrepresented in the literature.

Methods

This single-institution study included 107 patients with large lesions treated between 2004 to 2012. 44 patients with medium (2 to ≤5 cm) were compared to 47 with large (5 to ≤10 cm), and 16 with very large (>10 cm) lesions. Radiation was radiobiologically-guided and ranged from 29 to 88 Gy in 5 to 25 fractions. Acute and late toxicity was prospectively collected at one-month post RT, and then every three months.

Figure 1: Progression free survival by lesion size

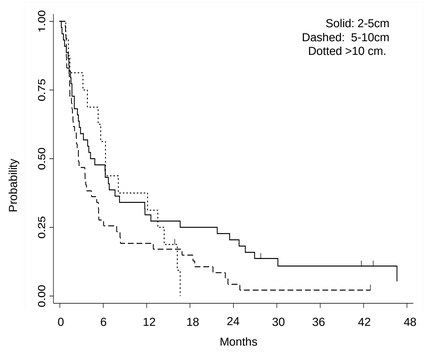
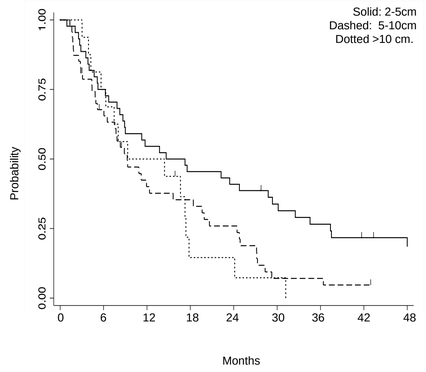


Figure 2: Overall survival by lesion size



Results

Table 1: Characteristics of the study population

	All Lesions n=107	2-5cm n=44	5-10cm n=47	>10cm n=16	p value for chi² or ANOVA
Age (y)					
Mean	67.4	66.4	67.7	69.3	p=0.6982
Range	22-89	22-89	48-88	50-82	
Sex					
Male	67 (62.6)	24 (54.6)	32 (68.1)	11 (68.8)	p=0.353
Female	40 (37.38)	20 (45.5)	15 (31.9)	5 (31.3)	
Intrahepatic lesions					
1	47 (43.9)	17 (38.6)	23 (48.9)	7 (43.8)	p=0.247
2	21 (19.6)	10 (22.7)	9 (19.2)	2 (12.5)	
3	18 (16.8)	11 (25.0)	6 (12.8)	1 (6.3)	
4	10 (9.4)	3 (6.8)	3 (6.4)	4 (25.0)	
5 +	11 (10.3)	3 (6.8)	6 (12.8)	2 (12.5)	
Primary Cancer					
HCC	44 (41.1)	9 (20.5)	25 (53.2)	10 (62.5)	**p=0.001**
Metastasis	63 (58.9)	35 (79.6)	22 (46.8)	6 (37.5)	
Child-Pugh Class					
A	82 (76.6)	36 (81.8)	36 (76.6)	10 (62.5)	p=0.345
B	24 (22.4)	7 (15.9)	11 (23.4)	6 (37.5)	
C	1 (0.9)	1 (2.3)	0 (0.0)	0 (0.0)	
Extrahepatic Disease					
Yes	46 (43.0)	23 (52.3)	17 (36.2)	6 (37.5)	p=0.268
No	61 (57.0)	21 (47.7)	30 (63.8)	10 (62.5)	
Previous chemotherapy					
Yes	52 (48.6)	29 (65.9)	17 (36.2)	6 (37.5)	**p=0.011**
No	55 (51.4)	15 (34.1)	30 (63.8)	10 (62.5)	
Previous chemo-embolization					
Yes	15 (14.0)	4 (9.1)	9 (19.2)	2 (12.5)	p=0.378
No	92 (86.0)	40 (90.1)	38 (80.8)	14 (87.5)	

Table 2: Treatment summary

	All Lesions n=107	2-5cm n=44	5-10cm n=47	>10cm n=16
Prescribed dose (Gy)				
Median	50.10	55.40	47.25	39.65
Range	29.40-87.75	30.00-87.75	27.50-78.00	29.40-57.00
Number of fractions				
5-6	37 (34.6)	14 (31.8)	18 (38.3)	11 (68.8)
10-25	70 (65.4)	30 (68.2)	29 (61.7)	5 (31.3)
EQD2Gy (Gy)				
Median	57.7	72.2	55.4	43.0
Range	32.5-133.2	40.0-133.2	35.5-100	32.5-65.9

Table 3: Univariate and multivariate analysis of PFS

Variable		Univariate			Multivariate		
	Continuous/ reference group	HR	95% CI	P	HR	95% CI	P
Age	Continuous	0.995	0.984-1.005	0.306			
Gender (male)	Female	1.391	0.925-2.093	0.113			
Multiple lesions	No	1.137	0.765-1.691	0.525			
Diagnosis (HCC)	Other	0.873	0.585-1.302	0.505			
CPS B or C	A	1.458	0.920-2.310	0.108			
Extrahepatic disease	No	1.547	1.039-2.305	**0.032**	1.414	0.921-2.170	0.113
Previous chemotherapy	No	1.236	0.832-1.837	0.294			
Previous chemo-embolization	No	0.519	0.288-0.934	**0.029**	0.376	0.202-0.702	**0.002**
EQD2Gy (Gy)	Continuous	0.986	0.977-0.995	**0.002**	0.987	0.976-0.998	**0.023**
Size							
2-5cm	2-5cm	-	-	-			
5-10cm	2-5cm	1.615	1.044-2.499	**0.031**	1.607	0.978-2.640	0.061
>10cm	2-5cm	1.205	0.654-2.224	0.549	0.844	0.426-1.670	0.626

Table 4: Univariate and multivariate analysis of OS

Variable		Univariate			Multivariate		
	Continuous/ reference group	HR	95% CI	P	HR	95% CI	P
Age	Continuous	1.004	0.992-1.015	0.521			
Gender (male)	Female	0.851	0.557-1.300	0.454			
Multiple lesions	No	0.865	0.574-1.302	0.486			
Diagnosis (HCC)	Other	1.044	0.693-1.572	0.838			
CPS B or C	A	3.128	1.906-5.135	**0.000**	3.208	1.855-5.548	**0.000**
Extrahepatic disease	No	1.257	0.831-1.900	0.270			
Previous chemotherapy	No	0.949	0.632-1.423	0.800			
Previous chemo-embolization	No	0.502	0.273-0.924	**0.027**	0.429	0.228-0.804	**0.008**
EQD2Gy (Gy)	Continuous	0.984	0.974-0.994	**0.001**	0.984	0.973-0.995	**0.004**
Size							
2-5cm	2-5cm	-	-	-			
5-10cm	2-5cm	1.771	1.122-2.795	**0.014**	1.715	1.057-2.781	**0.029**
>10cm	2-5cm	1.933	1.035-3.607	**0.038**	0.825	0.402-1.696	0.601

Patient and Treatment Characteristics (Table 1 & 2)

•Our series included 44 HCC and 63 METs patients. Median diameter of medium, large, and very large lesions was 3.5, 7.0, and 13 cm, respectively. Child-Pugh (CP) class was A, B, and C in 77%, 22% and 1% of patients, respectively.

Disease Control (Table 3)

•PFS was 26% at 12 months and 11% at 24 months. On univariate analysis, significant factors affecting PFS were extrahepatic disease, previous chemoembolization and large lesion status.

•However, only EQD2 and previous chemoembolization remained significant on multivariate analysis.

Overall Survival (Table 4)

•OS for cohort was OS for the cohort was 48% at 12 months and 31% at 24 months. On univariate analysis, factors significant to OS were: large lesions, very large lesions, CP of B or C, previous chemoembolization and equivalent dose in 2Gy fractions as a continuous variable.

•However, on multivariate analysis, very large lesions category was not a significant factor for OS.

Symptoms and Toxicities (Table 5 & 6)

•The most common toxicities were fatigue (n=45), abdominal pain (n=40), bleeding (n=2), and nausea (n=6).

•Change scores comparing symptoms before and after RT revealed stable or improved rates for all patients. Toxicity was not statistically different between different size categories at all time points. There were no grade 4 or 5 toxicities.

Table 5: Acute toxicities Chi^2: 0.918, P=0.992

RTOG	2-5cm n=44	5-10cm n=47	>10cm n=16
0	7 (16%)	5 (11%)	2 (13%)
1	16 (36%)	16 (34%)	6 (38%)
2	16 (36%)	20 (44%)	6 (38%)
3	5 (11%)	6 (13%)	2 (13%)

Table 6: Late toxicities Chi^2: 5.83, P=0.440

RTOG	2-5cm n=44	5-10cm n=47	>10cm n=16
0	19 (43%)	25 (53%)	7 (44%)
1	19 (43%)	25 (53%)	7 (44%)
2	8 (18%)	12 (26%)	5 (31%)
3	6 (14%)	6 (13%)	1 (6%)

Conclusion

Patients with larger lesions have a worse OS but experience a similar stability or improvement in symptom and toxicity scores with treatment. Individualized radiobiological constraints appear to result in the ability to treat large lesions safely.