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重新評估射頻燒灼術與手術切除在早期單發性肝上皮細胞癌之應用—南臺灣準醫學中心之十年經驗

Re-appraisal the Application of Radiofrequency Ablation and Surgical Resection in Early Solitary Hepatocellular Carcinoma

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Introduction

As the advance of locoregional and ablative treatment, there was little literature regarding the long term(> 10 years) effect of surgical resection(SR) and radiofrequency ablation(RFA) treatment between solitary hepatocellular carcinoma(HCC) < 2cm or 2-3 cm in diameter.

Materials and Methods

Retrospectively we have enrolled patients diagnosed with primary and solitary which HCCs of which primary diameter below 3 centimeter and apply SR(open or laparoscopic approach) or RFA as first line of treatment at E-Da hospital, the entire cohort is divided into 2 subgroups, namely 2cm and 2-3cm in diameter for statistical analysis.

		<2 cm (%)		2 - 3 cm (%)			p value
		N = 185	46.1	N = 216	53.9	OR 95% CI	
Age		60.4±1.1		61.2±0.7			0.56
Sex(M/F)		124/61		155/61			0
initial AFP	ng/mL	170.5±806.7		137.0±363.6			0.58
Viral Hepatitis							
Hepatitis B	n(%)	63	34.6	85	38.9	0.80.23 - 1.20	0.27
Hepatitis C	n(%)	89	48.1	54	25	2.781.82 - 4.24	<0.0001
Hepatitis B &C	n(%)	6	3.2	57	26.4	0.090.04 - 0.22	<0.0001
non	n(%)	26	14.1	21	9.7	1.520.82 - 2.8	0.18
Segments involved							
I	n(%)	1	0.5	2	0.9	0.580.05 - 6.43	0.66
II	n(%)	21	11.4	14	6.5	1.850.91 - 3.75	0.09
III	n(%)	17	9.2	17	7.9	1.180.59 - 2.39	0.64
IV	n(%)	20	10.8	26	12	0.890.48 - 1.65	0.7
V	n(%)	33	17.8	38	17.6	1.020.61 - 1.7	0.95
VI	n(%)	44	23.8	54	25	0.940.59 - 1.48	0.78
VII	n(%)	28	15.1	39	18.1	0.740.04 - 1.26	0.27
VIII	n(%)	20	10.8	26	12	0.890.48 - 1.65	0.7
Hepatectomy	n(%)	87	47	84	38.9		0.11
RFA	n(%)	98	53	132	61.1		

Table 1a: The epidemiologic data of solitary HCC <20mm or 20-30mm in size

		<2 cm (%)		2 - 3 cm (%)			p value
		N = 185	46.1	N = 216	53.9	OR 95% CI	
1 yr Recurrence	n(%)	2	1.1	1	0.5	2.350.21-26.1	0.6
5 yr Recurrence	n(%)	5	2.7	14	6.5	0.40.14-1.13	0.1
10 yr Recurrence	n(%)	78	42.2	90	41.7	1.020.69-1.52	0.92
Mean recurrent time	months	56.2±41.2		48.9±37.3			0.09
1 yr overall survival	n(%)	185	100	215	99.5	0.390.02-9.56	1
5 yr overall survival	n(%)	181	97.8	196	90.7	0.220.07-0.65	0.003
10 yr overall survival	n(%)	128	69.2	119	55.1	0.360.24-0.55	<0.000001
1yr disease free survival	n(%)	165	89.2	196	90.6	1.190.61-2.30	0.61
5yr disease free survival	n(%)	106	57.2	116	53.7	0.860.58-1.28	0.47
10 yr disease free survival	n(%)	31	16.8	23	10.7	0.590.33-1.06	0.07

Table 1b: The oncologic outcome between solitary HCC <20mm or 20-30mm in size

		Hepatectomy(%)		RFA (%)		OR	95% CI	p value
		N= 171	42.6	N=230	57.4			
Age		57.5±0.9		63.6±0.7				<0.0001
Sex(M/F)		127/44		152/78				0.078
initial AFP	ng/mL	216.4±858.1		105.1±309.8				0.07
Viral Hepatitis								
Hepatitis B	n(%)	80	46.8	80	34.8	1.651.10 - 2.47		0.016
Hepatitis C	n(%)	58	33.9	106	46.1	0.60.40 - 0.90		0.015
Hepatitis B &C	n(%)	10	5.8	7	3	1.980.74 - 5.31		0.18
non	n(%)	23	13.5	37	16	0.810.46 - 1.42		0.46
Segments involved								
I	n(%)	2	1.1	1	0.4	2.710.24 - 30.13		0.42
II	n(%)	13	7.6	22	9.6	0.780.38 - 1.59		0.49
III	n(%)	18	10.5	16	7	1.570.78 - 3.18		0.21
IV	n(%)	21	12.3	25	10.9	1.150.62 - 2.13		0.66
V	n(%)	31	18.1	40	17.4	1.050.63 - 1.76		0.85
VI	n(%)	47	27.5	52	22.6	1.30.82 - 2.05		0.26
VII	n(%)	20	11.7	47	20.4	0.520.29 - 0.91		0.02
VIII	n(%)	19	11.1	27	11.7	0.960.51 - 1.79		0.89

Table 2a: The epidemiologic data of solitary HCC receive hepatectomy or RFA

		hepatectomy(%)		RFA (%)		OR	95% CI	p value
		N= 171	42.6	N=230	57.4			
1 yr Recurrence	n(%)	0	0	3	1.3	0.18	0.01-3.53	0.26
5 yr Recurrence	n(%)	5	2.9	15	6.5	0.43	0.15-1.21	0.11
10 yr Recurrence	n(%)	69	40.4	100	43.5	0.88	0.59-1.31	0.54
Mean recurrent time	months	31.1±22.0		28.4±17.4				0.39
1 yr overall survival	n(%)	171	100	229	99.6	0.45	0.02-11.01	1
5 yr overall survival	n(%)	167	97.7	210	91.3	0.25	0.08-0.75	0.009
10 yr overall survival	n(%)	132	77.2	115	50	0.3	0.19-0.46	<0.000001
1yr disease free survival	n(%)	156	91.5	208	90.3	0.9	0.46-1.81	0.79
5yr disease free survival	n(%)	92	53.7	131	57	1.1	0.76-1.70	0.53
10yr disease free survival	n(%)	29	16.9	8	5.8	0.18	0.08-0.40	<0.0001

Table 2b: The oncologic outcome of solitary HCC receive hepatectomy or RFA

Results

A total of 420 patients was included. 19 patients were excluded from our analysis based on our exclusion criteria, among these patients, 12 of them were cholangiocarcinoma at the final pathology, another 5 patients were found to be chronic inflammation and/or chronic inflammations. Lastly, 4 of these patients received liver transplantation during follow up period. Therefore a total of 401 patients was enrolled into the final analysis.

Prior to analyze primary outcome, the comparison of epidemiologic data between solitary HCCs sized below 20mm in diameter and between 20mm to 30mm were shown in Table. 1a.

The patients with primary tumor diameter below 20mm showed higher 5th year and 10th year overall survival(OS) (5th year OS: 97.8% v.s 90.7%, p = 0.003; 10th year OS: 69.2% v.s 55.1%, p <0.000001). (Table 1b)

There are no difference in mean recurrence months and rate at 1st, 5th, 10th year after receiving initial treatment in both tumor size below 20mm and between 20 – 30mm subgroups.

When study cohort was divided by received initial HCC treatments, the results are showed in Table. 2a. The primary lesions at segment VII were more prone to receive RFA than SR(11.7% v.s 20.4%, OR: 0.52, 95% CI: 0.29 – 0.91, p = 0.02).

There are no significance in comparing mean recurrent time and recurrence in 1st, 5th and 10th year after primary treatment in both SR and RFA subgroups.
(Mean recurrent time: 31.1 ± 22.0 months v.s 28.4 ± 17.4 months, p = 0.39)(Table. 2b)

At the subgroup of age above 75 years old, there are no benefit in recurrent time. Additionally, the patients aged above 75 who received SR still showed higher rates of OS and DFS at 10th year post treatment, while none of the RFA counterparts survived at that timeframe(10th year OS: 50% v.s 0%, p = 0.004; 10th year DFS: 30% v.s 0%, p = 0.018).(Table 3a)

At the subgroup whose age below 75, higher overall survival rates in 1st, 5th and 10th year post primary treatment. When comparing OS and DFS between different subgroups of primary HCC diameter and received primary treatment, there are statistically significance in 5th and 10th year OS between SR and RFA group(5th yr OS: 85.7% v.s 58.7%, p = 0.01; 10th yr, p <0.0001).

When comparing primary tumor size below 2cm and 2-3cm in RFA subgroup, there is significant difference in overall survival at 5th and 10th year(5th yr OS: 90.3% v.s 58.7%,p = 0.005; 10th yr OS: 64.3% v.s 39.4%, p = 0.0002), (Table 3a.). Higher 10th year disease-free survival rate in hepatectomy subgroup (82.75% v.s 59.80%, p = 0.0005)(Table 3b).

Using Kaplan – Meier survival curve analysis, the benefit of SR in overall survival(OS) only showed statistical significance in patients age < 75, there was no significance between SR and RFA in the subgroup of patients age > 75 years old.

	Hepatectomy	(%)	RFA	(%)	p value	OR	95% CI
below 2 cm	5yr OS	50.00%	5yr OS	87.50%	0.27	0.14	0.00 - 4.61
	10yr OS	50.00%	10 yr OS	35.00%	0.75	1.67	0.07 - 37.73
2-3 cm	5yr OS	50.00%	5yr OS	16.60%	0.06	4.83	0.94 - 24.95
	10yr OS	50.00%	10yr OS	0.00%	0.007	71	3.26 - 1547.96
Compare 5yr and 10 yr overall survival of solitary HCCs < 2cm in size and 2-3cm in size							
p value	5yr	1	5yr	0.002			
(<2 to 2-3: OS)	10yr	1	10yr	0.02			
OR	5yr	1	5yr	0.03			
(<2 to 2-3: OS)	10yr	1	10yr	0.02			
95% CI	5yr	0.05 - 22.2	5yr	0.00 - 0.29			
(<2 to 2-3: OS)	10yr	0.05 - 22.2	10yr	0.00 - 0.49			

Table 3a: The overall survival in solitary HCC patients age > 75

	Hepatectomy	(%)	RFA	(%)	p value	OR	95% CI
below 2 cm	5yr OS	85.90%	5yr OS	65.30%	0.016	0.29	0.11 - 0.79
	10yr OS	72.20%	10yr OS	55.40%	0.056	0.44	0.19 - 1.02
2-3 cm	5yr OS	82.40%	5yr OS	46.40%	<0.0001	0.18	0.09 - 0.32
	10yr OS	70.10%	10yr OS	31.80%	<0.0001	0.2	0.11 - 0.34
Compare 5yr and 10 yr overall survival of solitary HCCs < 2cm in size and 2-3cm in size							
p value	5yr	0.54	5yr	0.03			
(<2 to 2-3: OS)	10yr	0.69	10yr	0.006			
OR	5yr	0.75	5yr	0.46			
(<2 to 2-3: OS)	10yr	0.86	10yr	0.39			
95% CI	5yr	0.29 - 1.9	5yr	0.23 - 0.91			
(<2 to 2-3: OS)	10yr	0.41 - 1.79	10yr	0.20 - 0.76			

Table 3b: The overall survival in solitary HCC patients age < 75

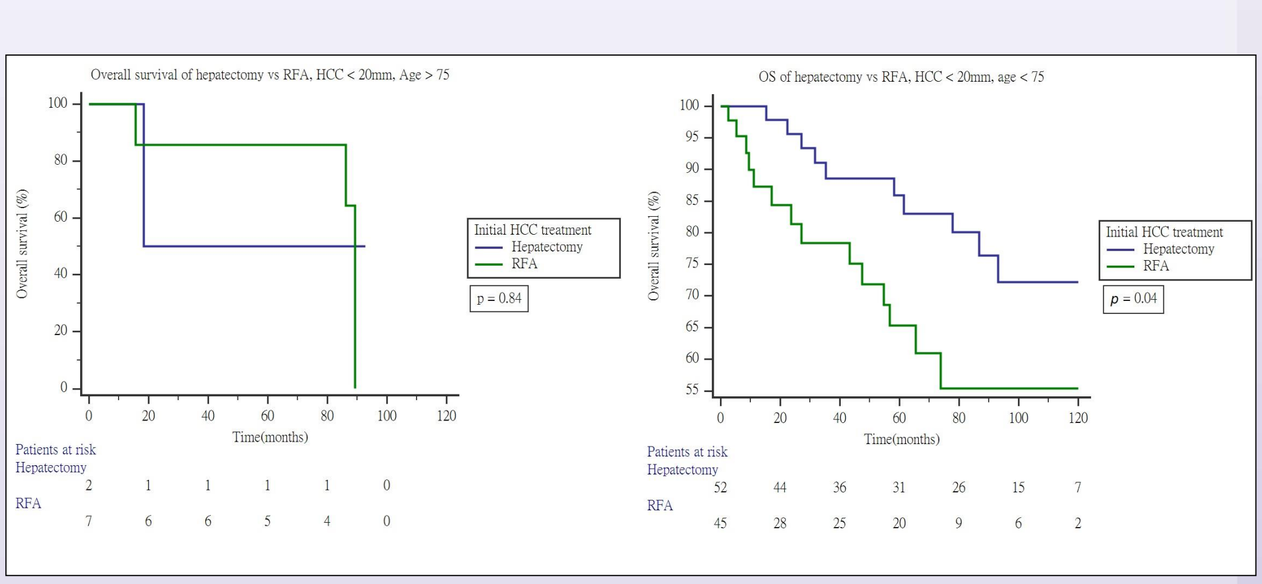

Figure 1: Comparison of overall survival between HCC < 20mm, Age above or below 75 y/o

Conclusion

S7 HCCs, elders and HCV patients are prone to receive RFA. Although SR and RFA share similar recurrence in HCC < 30mm within 10 years, SR still has better 10 yr OS in both HCC <20mm and 20-30mm. Age is a key factor to determine oncology outcome between SR & RFA (In solitary HCC < 20mm). Patients younger than 75 y/o seemed to sustain more beneficial effect from SR (or life expectancy > 10 yrs).