



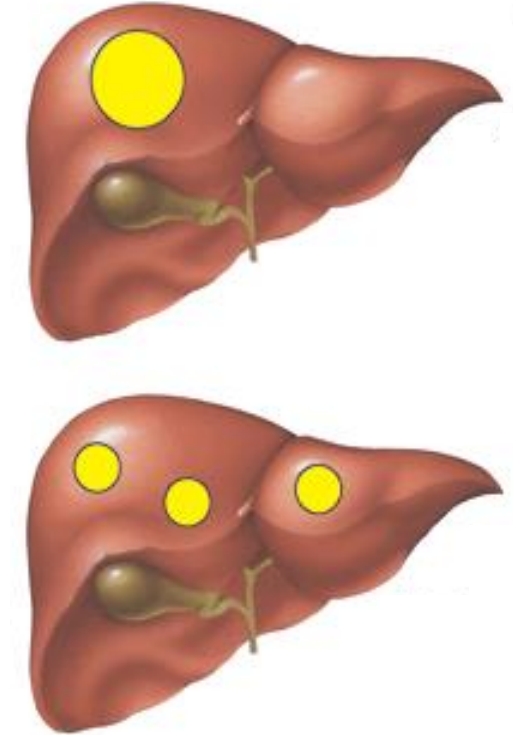
Liver-directed combined radiotherapy for downstaging of over the Milan hepatocellular carcinoma converting to liver transplantation

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Introduction

- Curative surgery; R0 resection, Liver transplantation
 - Best opportunity for achieving **long-term survival in HCC**
- LT eligibility; Milan criteria
 - Single tumor, not > 5cm
 - Up to 3 tumors, non > 3cm
 - Absence of macroscopic vascular invasion or extrahepatic spread

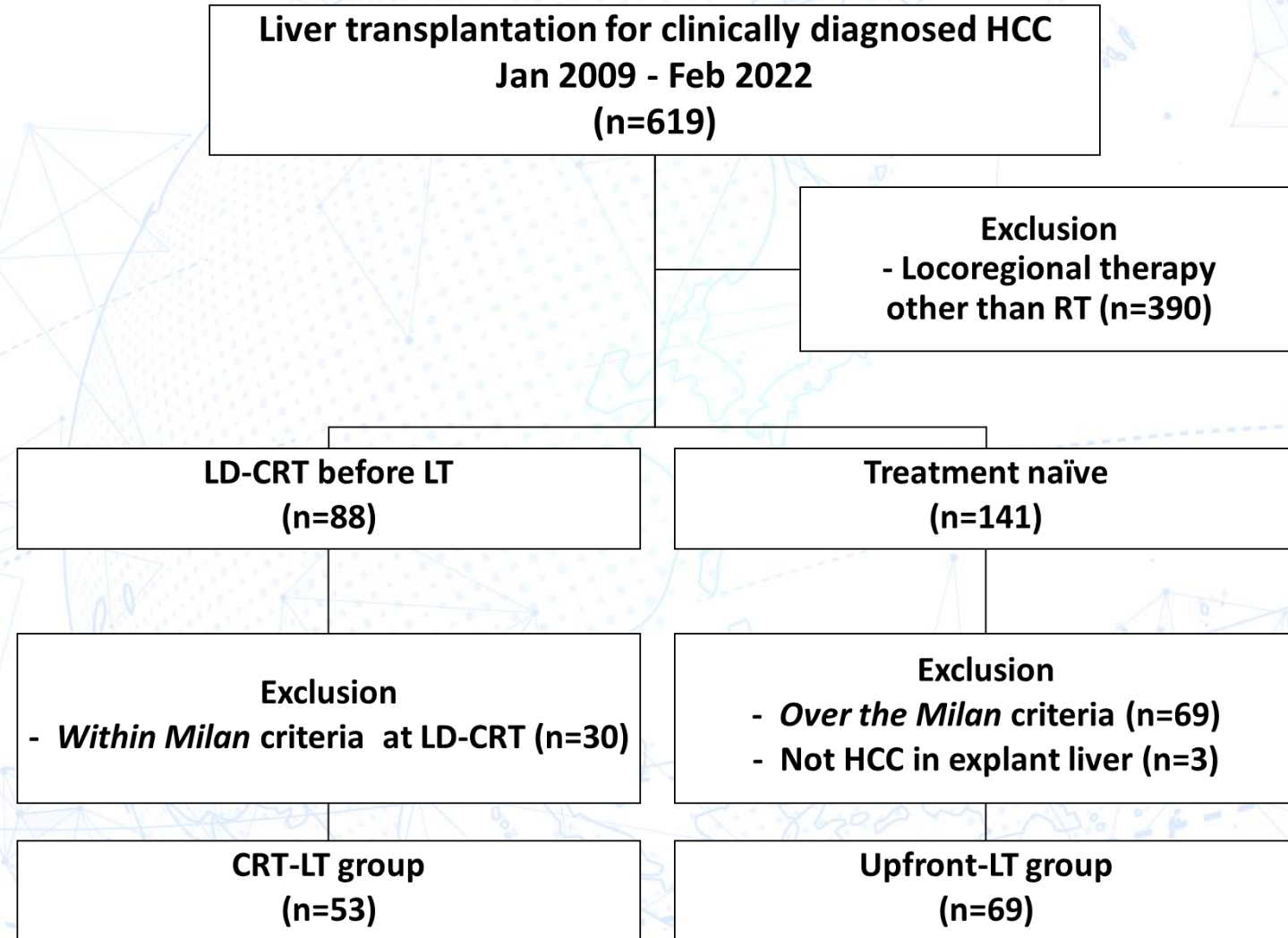


Purpose of this study

- To investigate the role of **Liver-directed combined radiotherapy(LD-CRT)** as a **downstaging strategy** of over the Milan HCC converting to LT.

Materials and Methods

- Inclusion criteria
 - From Jan 2009 to Feb 2022
 - Clinically diagnosed HCC undergone LT
- Comparison of Upfront-LT group and CRT-LT group
- Endpoint : Overall survival(OS), recurrence-free survival(RFS)



Patient characteristics

Characteristics	N (%)			p-value
	All patients (n=122)	Upfront-LT (n=69)	CRT-LT (n=53)	
Age (yrs)				
median (range)	56 (36 - 73)	56 (38 - 73)	55 (36 - 69)	0.056
Sex				0.138
Male	93 (67.2)	49 (71)	44 (83)	
Female	29 (23.8)	20 (29)	9 (17)	
Viral etiology				0.001
HBV	91 (74.6)	43 (62.3)	48 (90.6)	
HCV	10 (8.2)	10 (14.5)	0 (0)	
Non-viral	21 (17.2)	16 (23.2)	5 (9.4)	
CTP class				<0.001
A	72 (59)	24 (34.8)	48 (90.6)	
B	39 (32)	34 (49.3)	5 (9.4)	
C	11 (9)	11 (15.9)	0 (0)	
Tumor marker				
AFP (ng/mL)	16 (0.83 - 120000)	9 (0.83 - 2743.8)	95.8 (1.3 - 120000)	0.01
PIVKA-II (mAU/mL)	73.5 (5 - 75000)	35 (5 - 1112)	417.5 (10 - 75000)	0.05

Patient characteristics

Characteristics	N (%)			p-value
	All patients (n=122)	Upfront-LT (n=69)	CRT-LT (n=53)	
Tumor size (largest diameter in cm)				
median(range)	2.8 (0.8 - 16.8)	2.1 (0.8 - 4.8)	6.3 (1 - 16.8)	<0.001
No. of lesions				
median(range)	1 (1 - 12)	1 (1 - 3)	2 (1 - 12)	<0.001
Vascular invasion		0 (0)	39 (73.6)	
Extrahepatic lesion		0 (0)	6 (11.3)	
Stage				<0.001
I	30 (24.6)	30 (43.5)	0 (0)	
II	45 (36.9)	33 (47.8)	12 (22.6)	
III	27 (22.1)	6 (8.7)	21 (39.6)	
IVA	19 (15.6)	0 (0)	19 (35.8)	
IVB	1 (0.8)	0 (0)	1 (1.9)	
Previous treatments				
No	93 (76.2)	69 (100)	24 (45.3)	
Yes	29 (23.7)	0 (0)	29 (54.7)	

Treatment characteristics (CRT-LT, N=53)

Characteristics	N	%
LD-CRT		
*iA-CCRT	41	77.3
*TACE + RT	10	18.9
*RFA + RT	1	1.9
RT alone	1	1.9
Dose scheme		
Conventional fractionation	50	94.3
Hypofractionation	3	5.6
SBRT	1	1.9
Modality		
3D CRT	10	18.9
IMRT	43	81.1

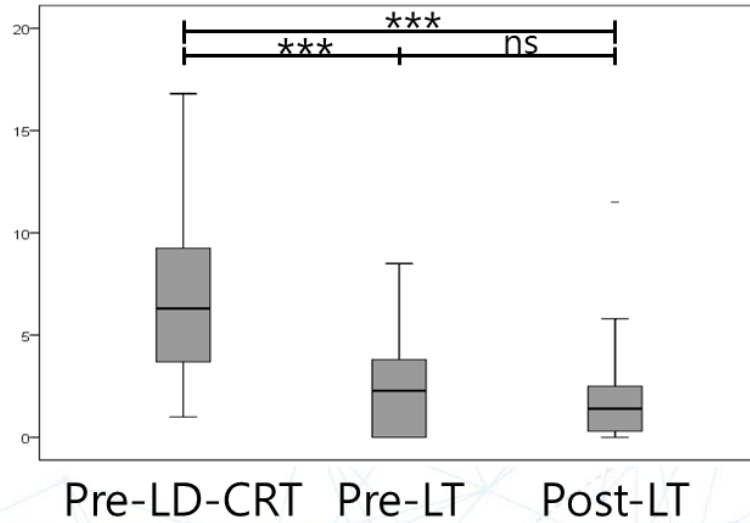
Characteristics	
No. of fractions	
median (range)	25 (10 – 30)
BED (Gy, $\alpha/\beta=10$)	
median (range)	123 (42.48 – 150)

- * TACE : Transcatheter arterial chemoembolization
- * RFA : Radiofrequency ablation
- * iA-CCRT: Concurrent chemoradiation therapy (concurrent HAIC + RT)
- * HAIC : Hepatic arterial infusion chemotherapy

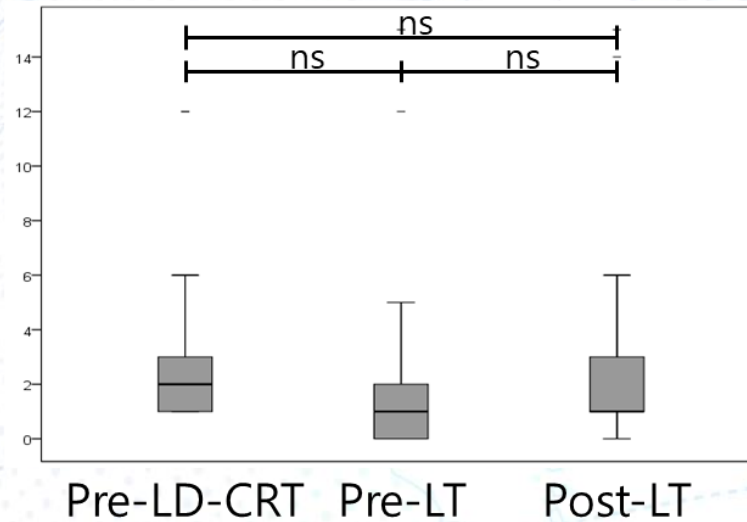
- * SBRT : Stereotactic body radiation therapy
- * IMRT : Intensity modulated radiation therapy
- * 3D CRT : 3-dimensional conformal radiation therapy
- * BED: Biologically effective dose

Change in tumor status after LD-CRT (N=53)

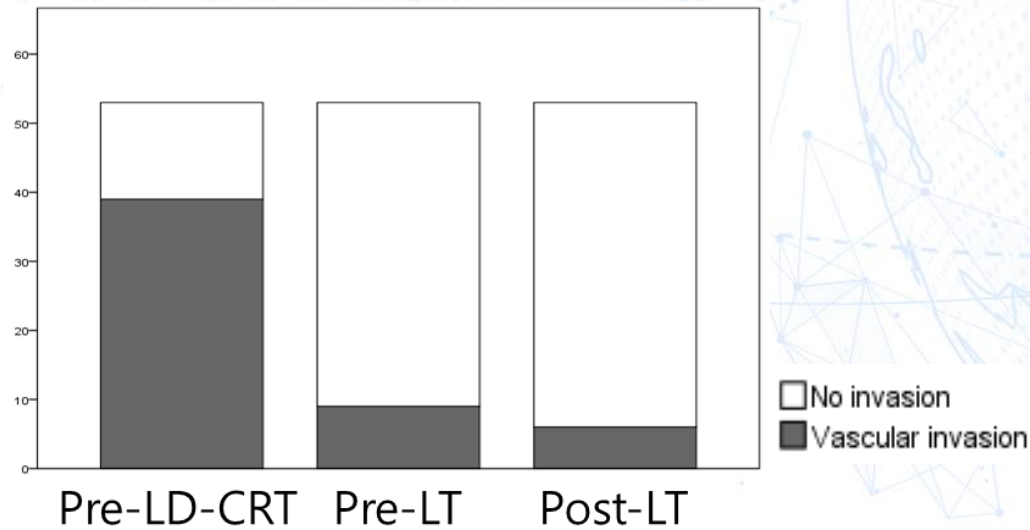
Tumor size (Largest diameter in cm)



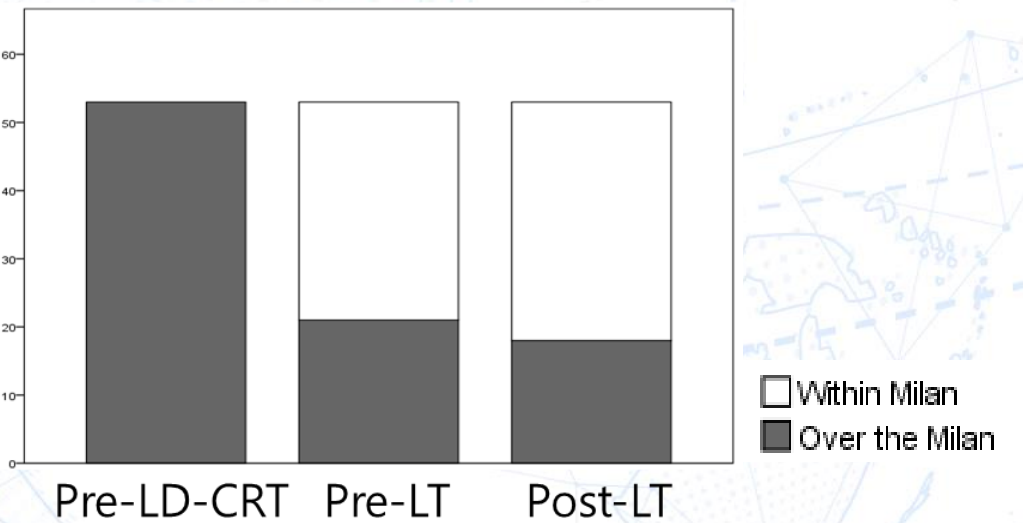
No of lesions



No of pts with vascular invasion



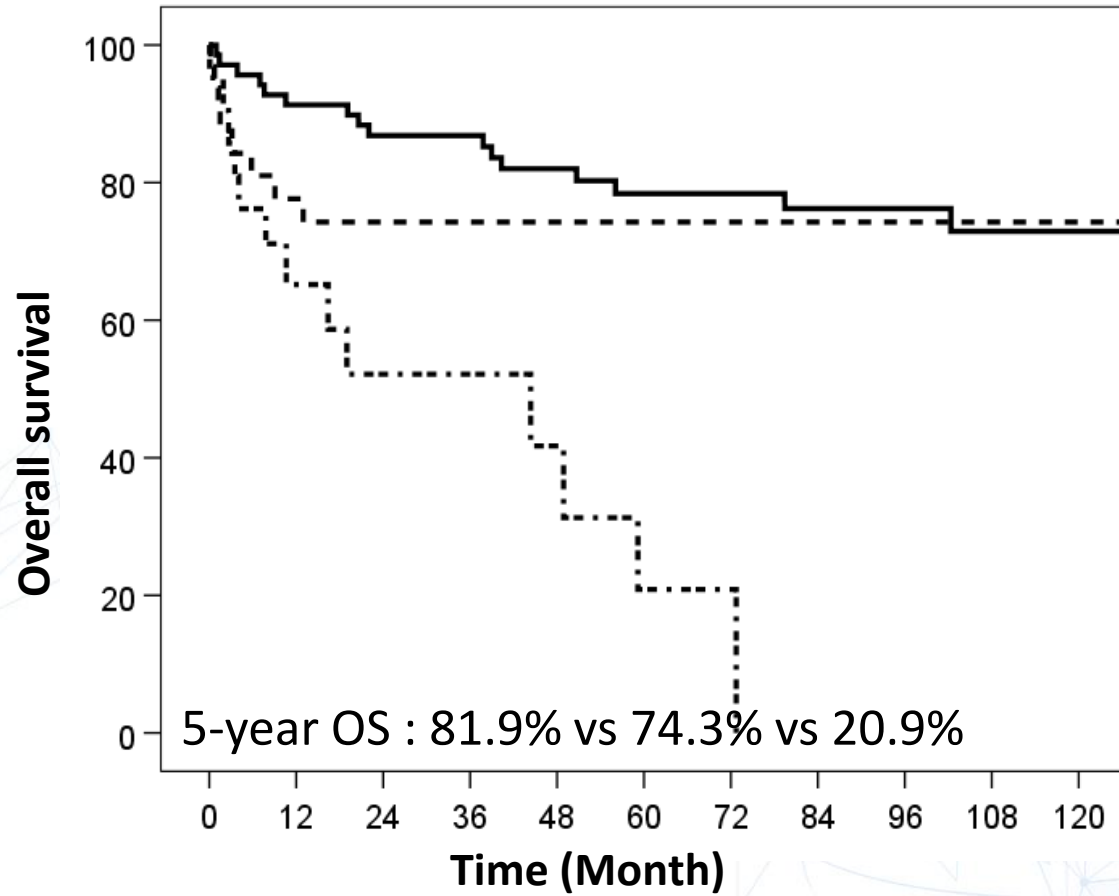
No of pts *within Milan*



Substantial **downstaging** to *within Milan* has been achieved in **66%** of patients.

Comparison of OS and RFS

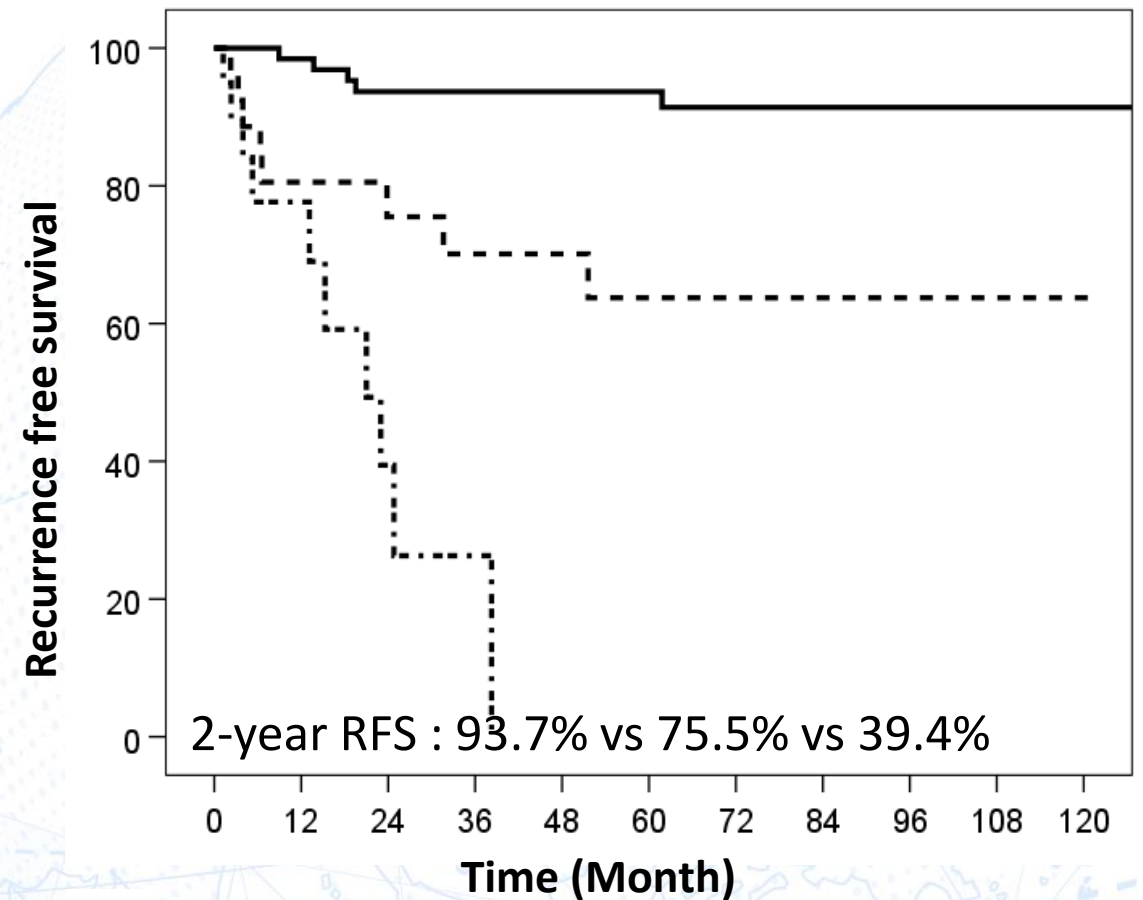
Overall survival since LT



Legend for Overall survival:
— Upfront-LT
- - CRT-LT (Downstaged to Milan)
... CRT-LT (Not downstaged)

Statistical significance:
Upfront-LT vs CRT-LT (Downstaged to Milan): $p=0.219$
Upfront-LT vs CRT-LT (Not downstaged): $P=0.008$
CRT-LT (Downstaged to Milan) vs CRT-LT (Not downstaged): $P<0.001$

Recurrence free survival since LT



Legend for Recurrence free survival:
— Upfront-LT
- - CRT-LT (Downstaged to Milan)
... CRT-LT (Not downstaged)

Statistical significance:
Upfront-LT vs CRT-LT (Downstaged to Milan): $p=0.001$
Upfront-LT vs CRT-LT (Not downstaged): $P=0.008$
CRT-LT (Downstaged to Milan) vs CRT-LT (Not downstaged): $P<0.001$

Successfully downstaged patients showed **similar survival but higher postLT recurrence** than those in upfront-LT group.

Conclusion

- Liver-directed combined radiotherapy seems effective as a **downstaging strategy for liver transplantation** in advanced hepatocellular carcinoma patients.