Supplementary material

Supplementary Table 1 Recurrence pattern in the total relapsed population

Variables	**Total (n = 252)**	**non-TO (n = 80)**	**TO (n = 172)**	***P***
Recurrence site [a]				0.008
Intrahepatic	157 (62.30)	40 (50.00)	117 (68.02)	
Extrahepatic	46 (18.25)	16 (20.00)	30 (17.44)	
Intra-and-extrahepatic	49 (19.44)	24 (30.00)	25 (14.53)	
Recurrence timing [a]				<.001
Early	120 (47.62)	54 (67.50)	66 (38.37)	
Intermediate	56 (22.22)	10 (12.50)	46 (26.74)	
Later	76 (30.16)	16 (20.00)	60 (34.88)	
Recurrence treatment [a]				<.001
Liver resection	51 (20.24)	2 (2.50)	49 (28.49)	
Liver ablation	24 (9.52)	6 (7.50)	18 (10.47)	
Systemic therapy	120 (47.62)	49 (61.25)	71 (41.28)	
Others	57 (22.62)	23 (28.75)	34 (19.77)	

Results in table are expressed as n (%).

a Percentage and comparison of those patients who recurrent.

Supplementary Table 2 Comparison of baseline characteristics between included and excluded patients

Variables	Excluded (n =48)	Included (n = 204)	*P*
Age, years	61.69±9.74	58.62±10.43	0.065
Gender			0.975
Male	18 (37.50)	77 (37.75)	
Female	30 (62.50)	127 (62.25)	
Tumor grade			0.002
Low	23 (47.92)	52 (25.49)	
High	25 (52.08)	152 (74.51)	
BMI, kg/m^2	23.97±3.51	23.46±3.29	0.342
Number of lesions	2.00 (1.00, 3.00)	2.00 (1.00, 3.00)	0.774
Max diameter, cm	2.95 (1.98, 4.08)	2.80 (1.95, 4.00)	0.710
CEA, ng/mL	10.12 (3.89, 37.14)	7.89 (3.51, 31.01)	0.315
Diabetes			0.865
No	43 (89.58)	181 (88.73)	
Yes	5 (10.42)	23 (11.27)	
Surgical approach			0.295
No	9 (18.75)	53 (25.98)	
Yes	39 (81.25)	151 (74.02)	
Neoadjuvant therapy			0.215
No	29 (60.42)	103 (50.49)	
Yes	19 (39.58)	101 (49.51)	
Major hepatectomy			0.351
No	41 (85.42)	186 (91.18)	
Yes	7 (14.58)	18 (8.82)	
Hypertension			0.195
No	25 (52.08)	127 (62.25)	
Yes	23 (47.92)	77 (37.75)	
Primary tumor location			0.350

Rectum	25 (52.08)	91 (44.61)	
Colon	23 (47.92)	113 (55.39)	
Lymph nodal metastasis			0.457
No	17 (35.42)	61 (29.90)	
Yes	31 (64.58)	143 (70.10)	
Synchronous			<.001
No	28 (58.33)	60 (29.41)	
Yes	20 (41.67)	144 (70.59)	
Distribution			0.897
Unilobar	32 (66.67)	134 (65.69)	
Bilobar	16 (33.33)	70 (34.31)	
ASA class			1.000
I-II	44 (91.67)	185 (90.69)	
III	4 (8.33)	19 (9.31)	
Simultaneous resection			0.249
No	37 (77.08)	140 (68.63)	
Yes	11 (22.92)	64 (31.37)	
Adjuvant therapy			0.184
No	16 (33.33)	49 (24.02)	
Yes	32 (66.67)	155 (75.98)	

Results in table are expressed as mean ± SD/ median (IQR)/n (%); BMI, body mass index; ASA, American society of anesthesiologists physical status; Synchronous*: Yes indicates synchronous metastasis, No indicates metachronous metastasis.

Supplementary Table 3 Uni- and multi-variable analysis of characteristics associated to the Textbook Outcome

Variables	Univariate		Multivariate	
	P	**OR (95%CI)**	***P***	**OR (95%CI)**
Gender, male	0.945	1.02 (0.55-1.88)		
Age, ≥ 60 years	0.809	1.08 (0.59-1.96)		
BMI, ≥ 24 kg/m^2	0.027	2.04 (1.08-3.83)	0.018	2.57 (1.18-5.62)
Hypertension	0.137	1.62 (0.86-3.05)		
Diabetes	0.598	1.30 (0.49-3.48)		
Tumor grade, High	0.308	1.41 (0.73-2.75)		
Laparoscopic	<.001	4.66 (2.40-9.08)	<.001	5.34 (2.36-12.08)
Major hepatectomy	0.023	0.32 (0.12-0.85)	0.118	0.37 (0.11-1.29)
Neoadjuvant therapy	0.006	2.37 (1.28-4.39)	0.234	1.56 (0.75-3.23)
Primary tumor location, colon	0.212	0.68 (0.37-1.25)		
Lymph nodal metastasis	0.957	1.02 (0.53-1.95)		
Synchronous	0.014	0.40 (0.19-0.83)	0.867	0.93 (0.38-2.28)
Multiple	0.577	1.19 (0.65-2.16)		
Bilobar	0.844	1.07 (0.57-2.00)		
Max diameter, > 3 cm	0.012	0.46 (0.25-0.84)	0.089	0.53 (0.25-1.10)
CEA, ≥ 10 ng/mL	0.875	0.95 (0.52-1.73)		
Simultaneous resection	<.001	0.23 (0.12-0.44)	<.001	0.19 (0.08-0.45)
Adjuvant therapy	0.963	0.98 (0.49-1.97)		
ASA, III	0.945	0.96 (0.35-2.67)		

OR, Odds Ratio; CI, Confidence Interval; BMI, body mass index; TO, textbook outcome; ASA, American society of anesthesiologists physical status; Synchronous*: Yes indicates synchronous metastasis, No indicates metachronous metastasis.

Supplementary Table 4 Sensitivity analysis: Association between Textbook Outcome (defined with alternative length-of-stay percentiles) and receipt of salvage curative-intent treatment

Definition of Prolonged LOS	TO Achieved	Univariable OR (95%CI)	*P* value	Multivariable OR (95%CI)	*P* value
> 75th percentile	141 (69.1)	5.43 (2.49–11.84)	<0.001	3.54 (1.52–8.25)	0.003
> 50th percentile	101 (49.5)	4.67 (2.51–8.67)	<0.001	3.59 (1.81–7.12)	<0.001
> 90th percentile	161 (78.9)	6.00 (2.24–16.02)	<0.001	4.24 (1.52–11.83)	0.006

OR, Odds Ratio; CI, Confidence Interval; LOS, length of stay; TO, Textbook Outcome

Supplementary Table 5 Sensitivity analysis: Univariable Cox regression of salvage curative-intent treatment at different landmark time points

Analysis	Patients excluded	HR	95% CI	*P*	Balance of baseline variables
Standard* (all patients)	0	0.284	0.155-0.520	<0.001	/
Landmark 6 months	6	0.301	0.164-0.553	<0.001	Balanced
Landmark 12 months	25	0.330	0.178-0.612	<0.001	Balanced
Landmark 18 months	58	0.404	0.195-0.840	0.015	Balanced

HR, Hazard ratio; CI, Confidence interval; SCT, salvage curative-intent treatment.

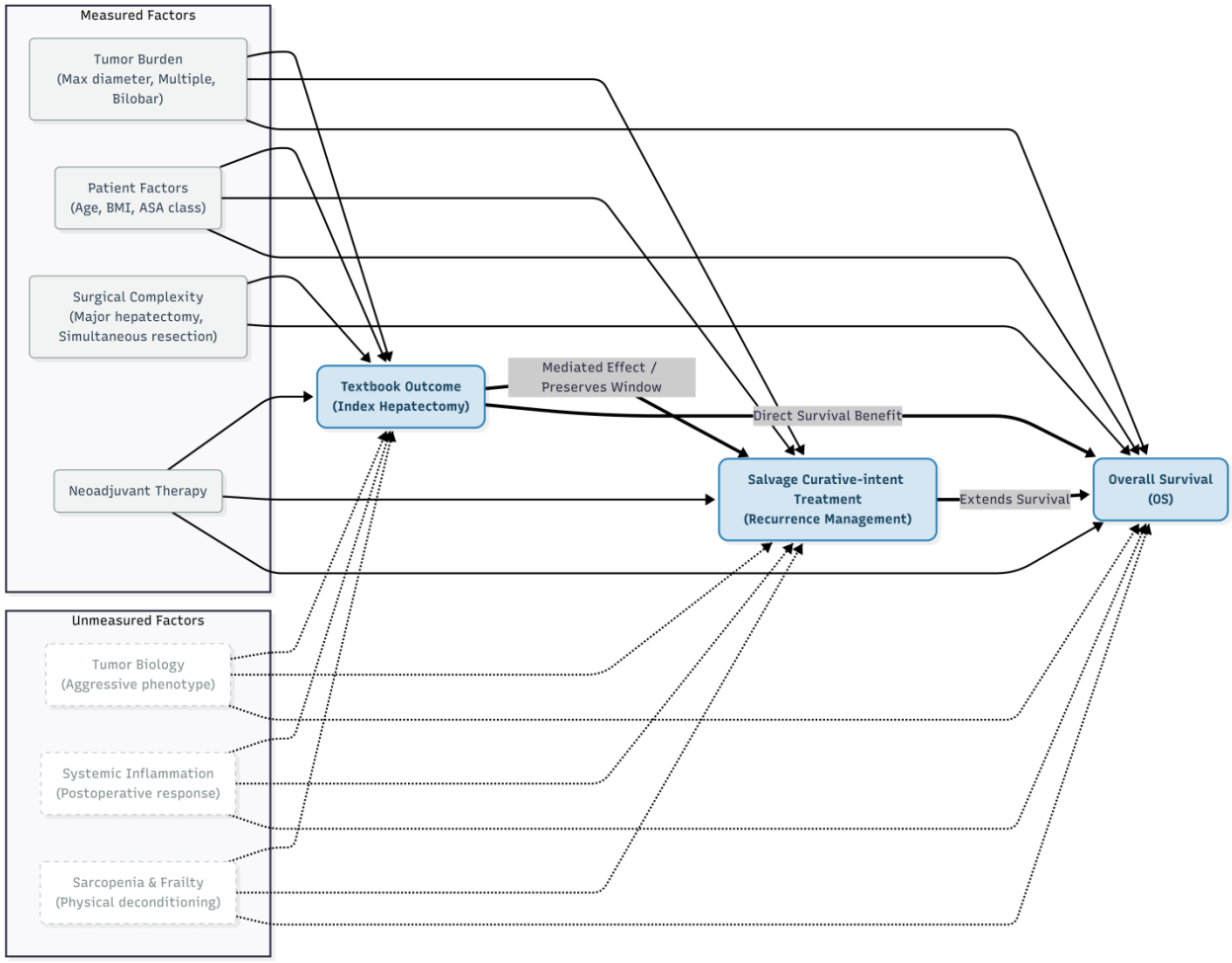
* The "Standard" analysis refers to the conventional univariable Cox regression without landmark adjustment, which includes all patients and is consistent with the initial baseline analysis. The Landmark analyses strictly excluded patients who died or were lost to follow-up prior to the specified time points (6, 12, and 18 months, respectively) to mitigate immortal time bias.

Supplementary Table 6 Proportional hazards assumption test using Schoenfeld residuals

Model	Test	*P*
Standard Cox (SCT)	Univariable	0.280
Landmark Cox (SCT)	Univariable	0.710
Landmark Cox	Multivariable	0.399
	GLOBAL	
TD-Cox (SCT)	Univariable	0.780
TD-Cox	Multivariable	0.101
	GLOBAL	

SCT, salvage curative-intent treatment; TD-Cox, time-dependent Cox regression.

Note:The proportional hazards assumption for each model was evaluated using the Schoenfeld residuals global test. A P value > 0.05 indicates no significant deviation from the assumption, thereby confirming that the proportional hazards assumption is perfectly satisfied for all presented univariable and multivariable models.



Supplementary Figure 1 Directed Acyclic Graph (DAG) illustrating the conceptual framework and hypothesized relationships among Textbook Outcome, Salvage Curative-intent Treatment, and Overall Survival. This DAG maps the clinical assumptions and biological hypotheses underlying the multivariable survival models in patients with colorectal liver metastases (CRLM). The central pathway evaluates the mediated and direct effects of achieving a Textbook Outcome (TO) at the index hepatectomy on Overall Survival (OS), particularly highlighting how an uncomplicated index surgery preserves the patient's eligibility for Salvage Curative-intent Treatment (SCT) upon recurrence.

Visual Key:

Solid blue boxes: Primary variables of interest (Exposure, Mediator, and Outcome).

Solid gray boxes: Measured baseline and surgical confounders that were adjusted for in the logistic and Cox proportional hazards regression models.

Dashed boxes: Unmeasured mechanistic factors (e.g., tumor biology, systemic inflammation, and sarcopenia) representing potential sources of residual confounding discussed in the manuscript.

Thick solid arrows: The primary hypothesized clinical pathways under investigation.

Thin solid arrows: Confounding paths from measured variables to the core variables.

Dashed arrows: Hypothesized confounding paths from unmeasured variables, underscoring the need for caution in causal interpretation.

Abbreviations: TO, Textbook Outcome; SCT, Salvage Curative-intent Treatment; OS, Overall Survival; BMI, Body Mass Index; ASA, American Society of Anesthesiologists.