SUPPLEMENTARY MATERIALS

Prognostic value of long non-coding RNAs MALAT1 in colorectal cancer patients: a pooled analysis of two cohorts.

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eTable 1. Detailed balance before and after propensity score adjustment in the initial cohort population.

Covariates	Higher MALAT1		Lower MALAT1		Std. Mean Diff.	
	Before	After	Before	After	Before	After
Propensity (all cases)	0.581	0.581	0.419	0.579	0.915	0.008
Gender(male vs. female)	0.512	0.512	0.622	0.492	-0.218	0.039
Age (yr)	58.122	58.122	58.134	58.621	-0.001	-0.046
Age_subgroup (≥60 vs. <60)	0.463	0.463	0.439	0.457	0.049	0.012
BMI (kg/m^2)	23.398	23.398	23.715	23.204	-0.103	0.063
BMI_subgroup (≥24 vs. <24)	0.476	0.476	0.463	0.363	0.024	0.225
Tumor Location						
Left colon vs. Right colon	0.305	0.305	0.232	0.256	0.158	0.106
Rectum vs. Right colon	0.585	0.585	0.646	0.610	-0.123	-0.050
Tumor size (mm)	61.000	61.000	53.646	57.986	0.212	0.087
CEA (ng/mL)	15.915	15.915	15.288	14.085	0.029	0.085
CEA-Group (>5 vs. ≤5)	0.537	0.537	0.451	0.455	0.170	0.163
CA199 (U/mL)	32.625	32.625	24.556	32.839	0.299	-0.008
CA199-Group (>37 vs. ≤37)	0.341	0.341	0.171	0.291	0.358	0.107
T-Stage						
T2 vs. T1	0.037	0.037	0.122	0.031	-0.452	0.031
T3 vs. T1	0.171	0.171	0.256	0.158	-0.225	0.034
T4 vs. T1	0.720	0.720	0.561	0.755	0.351	-0.077
N-Stage						
N1 vs. N0	0.329	0.329	0.463	0.297	-0.284	0.067
N2 vs. N0	0.061	0.061	0.049	0.044	0.051	0.072
M-Stage (M1 vs. M0)	0.061	0.061	0.134	0.107	-0.304	-0.192
Histopathological Morphology (infiltrating ulcer vs. protruding)	0.341	0.341	0.268	0.386	0.153	-0.093
Differentiation (high vs. low to medium)	0.378	0.378	0.366	0.375	0.025	0.006
Adjuvant Chemotherapy (yes vs. no)	0.415	0.415	0.341	0.431	0.148	-0.034

eTable 2. Detailed balance before and after propensity score adjustment in the external TCGA cohort population.

Covariates	**Higher MALAT1**		**Lower MALAT1**		**Std. Mean Diff.**	
	Before	**After**	**Before**	**After**	**Before**	**After**
Propensity (all cases)	0.523	0.523	0.477	0.523	0.461	0.001
Gender(male vs. female)	0.460	0.460	0.460	0.474	0.000	-0.029
Age (yr)	66.940	66.940	65.117	66.956	0.155	-0.001
Age_subgroup (≥60 vs. <60)	0.725	0.725	0.691	0.713	0.075	0.027
BMI (kg/m^2)	28.642	28.642	27.273	28.427	0.237	0.037
BMI_ subgroup (≥25 vs. <25)	0.735	0.735	0.611	0.723	0.281	0.028
Tumor Location						
Left colon vs. Right colon	0.383	0.383	0.372	0.378	0.021	0.009
Rectum vs. Right colon	0.215	0.215	0.191	0.219	0.057	-0.010
History of Polyps (yes vs. no)	0.346	0.346	0.289	0.380	0.120	-0.072
CEA (ng/mL)	18.582	18.582	17.183	20.536	0.054	-0.076
CEA-Group (>5 vs. ≤5)	0.597	0.597	0.520	0.606	0.157	-0.019
T-Stage						
T2 vs. T1	0.171	0.171	0.174	0.187	-0.009	-0.042
T3 vs. T1	0.681	0.681	0.691	0.641	-0.022	0.086
T4 vs. T1	0.114	0.114	0.101	0.139	0.042	-0.079
N-Stage						
N1 vs. N0	0.242	0.242	0.248	0.248	-0.016	-0.015
N2 vs. N0	0.205	0.205	0.171	0.185	0.083	0.048
M-Stage (M1 vs. M0)	0.178	0.178	0.121	0.159	0.149	0.050

eTable 3. Sensitivity analysis by using confounding RR analysis.

Populations	Models	HRs and 95% CIs for OS	Confounding RR (P-value)	HRs and 95% CIs for DFS	Confounding RR (P-value)
Initial cohort	Univariate	1.428 (0.901-2.263)	0.761 (0.181)	1.525 (0.975-2.387)	0.754 (0.082)
	PS-adjustment	1.087 (0.657-1.797)		1.150 (0.710-1.865)	
External cohort	Univariate	1.072 (0.750-1.532)	0.906 (0.873)	1.266 (0.948-1.690)	0.930 (0.057)
	PS-adjustment	0.971 (0.676-1.396)		1.177 (0.878-1.577)	
Combined populations	Univariate	1.194 (0.901-1.583)	0.846 (0.349)	1.337 (1.049-1.704)	0.875 (0.011)
	PS-adjustment	1.010 (0.752-1.355)		1.170 (0.910-1.502)	

eTable 4. Sensitivity analysis by using of conventional multivariate Cox hazard regression method.

Populations	Multivariate adjusted HR and 95% CI, P-value	
	OS	DFS
Initial cohort	1.037 (0.624-1.725), 0.888	1.261 (0.764-2.079), 0.364
External cohort	0.974 (0.674-1.408), 0.890	1.184 (0.883-1.587), 0.260
Combined populations	0.995 (0.739-1.341), 0.975	1.203 (0.934-1.550), 0.152

Initial cohort: OS anlaysis, adjusted for gender, age, BMI, AJCC stage, CA 19-9, adjuvant chemotherapy. DFS anslysis, adjusted for gender, age, BMI, AJCC stage, CA 19-9, CEA, tumor location, and adjuvant chemotherapy.

External cohort: OS analysis, adjusted for gender, age, BMI, tumor location, T stage, N stage, M stage, and CEA. DFS analysis, adjusted fro gender, age, BMI, T stage, N stage, M stage, and CEA.

eTable 5. Sensitivity analysis by excluding patients with shorter follow-up duration.

Sensitivity Analysis	Models	HR (95% CI), P-value	
		OS	DFS
Excluding patients with follow-up period ≤ 1 mo.	Univariate	1.055 (0.737-1.509), 0.770	1.254 (0.939-1.675), 0.126
	PS-adjustment	0.954 (0.663-1.373), 0.801	1.164 (0.868-1.561), 0.310
Excluding patients with follow-up period ≤ 3 mo.	Univariate	0.933 (0.640-1.358), 0.716	1.174 (0.872-1.581), 0.290
	PS-adjustment	0.856 (0.584-1.254), 0.424	1.101 (0.815-1.489), 0.530

eTable 6. Associations between MALAT1 expression level and clinical/pathological characteristics in the initial cohort population.

Factors	MALAT1 Expression Level		Univariate Model		Multivariate Model	
	Lower	Higher	OR (95% CI)	P-value	OR (95% CI)	P-value
Gender						
Female	51	42				
Male	31	40	1.567 (0.841-2.918)	0.157	1.525 (0.797-2.917)	0.202
Age (years)						
< 60	46	44				
≥ 60	36	38	1.104 (0.596-2.042)	0.754	1.090 (0.571-2.080)	0.795
BMI (kg/m^2)						
< 24	44	43				
≥ 24	38	39	1.050 (0.569-1.939)	0.876	1.108 (0.583-2.105)	0.755
Location site						
Right Colon	10	9				
Left Colon	19	25	1.462 (0.496-4.306)	0.491		
Rectum	53	48	1.006 (0.377-2.685)	0.990		
History of cancers						
No	69	73				
Yes	13	9	0.654 (0.263-1.628)	0.362		
Tumor Size (diameter, mm)						
≤ 40	31	27				
> 40	51	55	1.238 (0.652-2.351)	0.514		
CEA (ng/mL)						
≤ 5	45	38				
> 5	37	44	1.408 (0.762-2.603)	0.275		
CA19-9 (U/mL)						
≤ 37	68	54				
> 37	14	28	**2.519 (1.208-5.249)**	**0.014**	**2.522 (1.188-5.355)**	**0.016**
T-stage						
T1-3	36	23				
T4	46	59	**2.008 (1.048-3.845)**	**0.036**	**2.094 (1.072-4.090)**	**0.030**
N-stage						
N0	40	50				
N1 or N2	42	32	0.610 (0.328-1.133)	0.118		
M-stage						
M0	71	77				
M1	11	5	0.419 (0.139-1.266)	0.123		
Histopathological Morphology						
Protruding	60	54				
Infiltrating ulcer	22	28	1.414 (0.715-2.760)	0.310		
Differentiation						
Low to Medium	52	51				
High	30	31	1.054 (0.559-1.985)	0.872		

eTable 7. Associations between MALAT1 expression level and clinical/pathological characteristics in the external cohort population.

Factors	MALAT1 Expression Level		Univariate Model		Multivariate Model	
	Lower	**Higher**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Gender						
Female	137	137				
Male	161	161	1.000 (0.725-1.380)	1.000	0.952 (0.683-1.326)	0.770
Age (years)						
< 60	92	82				
≥ 60	206	216	1.176 (0.826-1.675)	0.368	1.218 (0.844-1.760)	0.292
BMI (kg/m^2)						
< 25	116	79				
≥ 25	182	219	**1.767 (1.249-2.500)**	**0.001**	**1.876 (1.313-2.679)**	**0.001**
Location site						
Right Colon	130	120				
Left Colon	111	114	1.113 (0.776-1.595)	0.562		
Rectum	57	64	1.216 (0.788-1.879)	0.377		
History of polyps						
No	212	195				
Yes	86	103	1.302 (0.921-1.841)	0.135	1.347 (0.941-1.928)	0.103
CEA (ng/mL)						
≤ 5	143	120				
> 5	155	178	1.368 (0.989-1.893)	0.058	1.356 (0.965-1.907)	0.080
T-stage						
T1-3	268	264				
T4	30	34	1.151 (0.684-1.934)	0.597		
N-stage						
N0	173	165				
N1 or N2	125	133	1.116 (0.807-1.543)	0.508		
M-stage						
M0	262	245				
M1	36	53	1.574 (0.996-2.488)	0.052	1.399 (0.865-2.264)	0.171

eTable 8. E-value analyses for the pooled effect estimates of the meta-analysis.

Outcome	Pooled HR (95% CI), P-value	E-values for	
		HR Point Estimate	HR Lower CI Limit
OS	1.683 (0.917-3.087), 0.093	2.221	1.000
DFS	1.784 (1.021-3.118) , 0.042	2.347	1.136

E-value shows the minimum strength of association that a hypothetical residual confounding factor would need to be associated with both the expression status of MALAT1 and the outcomes of CRC patients, and at the same time, the hypothetical confounding factor must be frequent to be able to fully explain the observed association between MALAT1 expression and CRC outcomes.