Supplementary Materials

Method S1. Inclusion and exclusion criteria

To develop mrDEC scoring system, LARC patients were retrospectively recruited from the five centers in China, including Guangdong Provincial People's Hospital (GDPH; Guangzhou, China), Shanxi Cancer Hospital (SXCH; Taiyuan, China), the Sixth Affiliated Hospital of Sun Yat-sen University (SYSU6; Guangzhou, China), Sun Yat-sen University Cancer Center (SYSUCC; Guangzhou, China), and Yunnan Cancer Hospital (YNCH; Kunming, China), served as Cohort1 (Figure S1). For the retrospective study, the inclusion criteria were as following: (i) All patients (aged ≥ 18 years) were pathologically diagnosed as rectal adenocarcinoma by electronic colonoscopy with biopsy and defined as locally advanced rectal cancer (cT3-4/N0-2, or EMVI+, or any T/N1-2, and M0) by enhanced pelvic magnetic resonance imaging (MRI);[1] (ii) All patients underwent standard neoadjuvant chemoradiotherapy (nCRT) regimen, followed by standard total mesorectal excision (TME) surgery; (iii) Pathological response [pathological complete response (pCR) vs. non-pCR] was confirmed by experienced pathologists after TME surgery; (iv) High-solution images of pretreatment MRI sequences, including axial T2-weighted imaging (T2WI), contrast enhanced T1-weighted imaging (CE-T1WI), and diffusion weighted imaging (DWI); MRI were performed within 2 weeks before the administration of nCRT; (v) No metastasis or other tumor events occurred during nCRT and operation. The exclusion criteria were as following: (i) A history of malignancy, chemoradiation therapy or surgery; (ii) Patients received nonstandard or incomplete nCRT, or had neoadjuvant chemo- or radiotherapy alone; (iii) No surgery or the pathological response evaluation of surgical specimen was unavailable; (iv) Lack of biopsy slides, or inadequate quality of WSI for analysis requirements (i.e., torn tissues, tissue folds, fade staining, or absence of tumor tissue); (v) Lack of images of pretreatment T2WI, DWI or CE-T1WI, or insufficient quality of MRI images to obtain measurements (i.e., motion artifacts).

For further validation, we performed a retrospective analysis of prospective trial. Eligible patients were prospectively recruited from the Sixth Affiliated Hospital of Sun Yat-sen University, Yunnan Cancer Hospital, Sir Run Run Shaw Hospital of Zhejiang University, and Nanfang Hospital of Southern Medical University (Fig. S1). For the prospective cohort (Cohort 2), only one inclusion criterion was added: All patients should have an Eastern Cooperative Oncology Group performance status ≤ 1 and adequate hematologic, liver, and renal function at recruitment.

Method S2. Neoadjuvant chemoradiotherapy treatment

All LARC patients received neoadjuvant radiotherapy concurrently given 5-fluorouracil based chemotherapy orally or intravenously. Induction chemotherapy before nCRT or consolidation chemotherapy after nCRT (5-fluorouracil based regimen combined with or without oxaliplatin, specifically for non-pCR patients) were implemented at physician's discretion. The neoadjuvant radiotherapy was delivered at 25 fractions of 2 Gy (gross tumor volume, GTV) and 1.8 Gy (clinical target volume, CTV) radiation, using Intensity-Modulated Radiation Therapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT) technique. A total dose of 50 Gy (GTV)/45 Gy (CTV) radiation was administered at 2.0 Gy/1.8 Gy per fraction, over a period (weekdays, day 1 to day 5) of 5 weeks. The TME surgery was performed within 6-8 weeks after the completion of nCRT, based on standard TME operation protocol. For the previous prospective trial, 4 (4%) patients were treated with local excision after evaluation by doctor.

Method S3. Clinical information collection

Clinical information was obtained from the medical records of the patients. The location of rectal cancer was categorized based on the distance of the tumor from the dentate line, with 0-5 cm classified as low rectal cancer, 5-10 cm as middle rectal cancer, and greater than 10 cm as high rectal cancer.[2] The reference range for the CEA level was established as 0-5 ng/ml.[3] TNM staging was performed in accordance with the standard criteria of the 8th TNM staging system.

Method S4. Pathological Treatment Response Evaluation

The TME surgery was undertaken after 6-8 weeks after completion of radiotherapy. Evaluation of H&E-stained slides of surgical resection specimen for residual tumor was performed under a standard reporting protocol in each participating hospital. The four categories of American Association of Cancer/College of American Pathologists (AJCC/CAP) tumor regression grading (TRG) system was employed to stratify the treatment response according to the volume of residual tumor cells: TRG 0 (complete response), no remaining viable cancer cells; TRG 1 (moderate response), only small cluster or single cancer cells remaining; TRG 2 (minimal response), residual cancer remaining with predominant fibrosis; TRG 3 (poor response), extensive residual cancer with minimal or no tumor killed [1]. We retrospectively collected data of TRG category from five centers. And data of TRG category of prospective trail was defined independently by two experienced gastroenterology pathologists, who were blinded to the clinicopathological information of patients. A third expert pathologist was responsible for the final decision in case of a disagreement between the two pathologists.

1. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rödel C, Cervantes A, et al. Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2017;28 suppl_4:iv22–40.

2. Jacobs L, Meek DB, van Heukelom J, Bollen TL, Siersema PD, Smits AB, et al. Comparison of MRI and colonoscopy in determining tumor height in rectal cancer. United European Gastroenterol J. 2018;6:131–7.

3. Kankanala VL, Mukkamalla SKR. Carcinoembryonic Antigen. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.

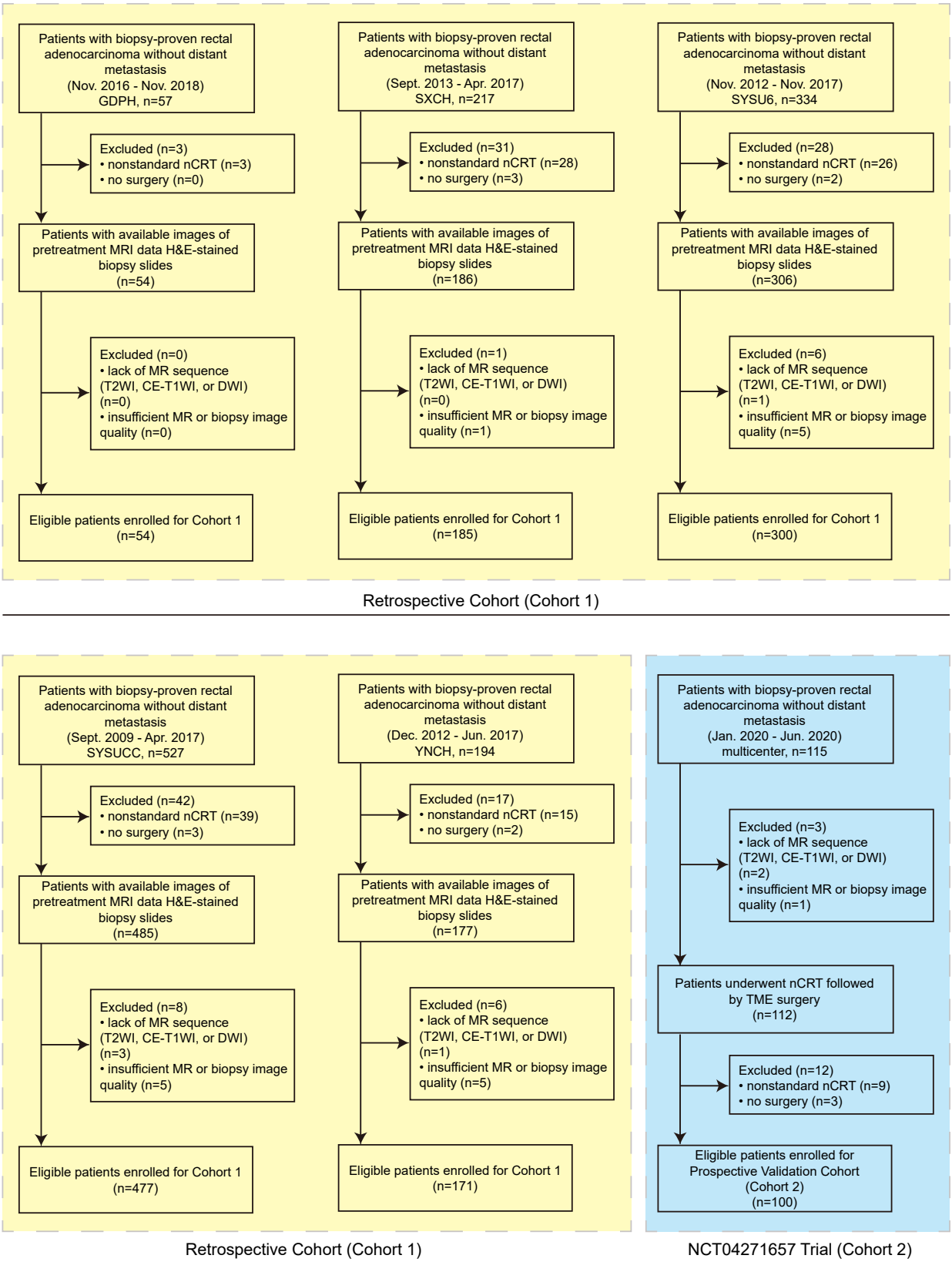

Figure S1. Patient enrollment for development of mrDEC scoring system. In the retrospective cohort patients were consecutively enrolled from five independent institutions (GDPH, Guangdong Provincial People's Hospital; SXCH, Shanxi Cancer Hospital; SYSU6, the Sixth Affiliated Hospital of Sun Yat-sen University; SYSUCC, Sun Yat-sen University Cancer Center; YNCH, Yunnan Cancer Hospital) and assigned into Cohort1. In the multicentre prospective observational clinical trial (NCT04271657), patients were prospectively recruited from four hospitals (the Sixth Affiliated Hospital of Sun Yat-sen University; Yunnan Cancer Hospital; Sir Run Run Shaw Hospital of Zhejiang University; Nanfang Hospital Southern Medical University), serving as the prospective cohort (Cohort2).

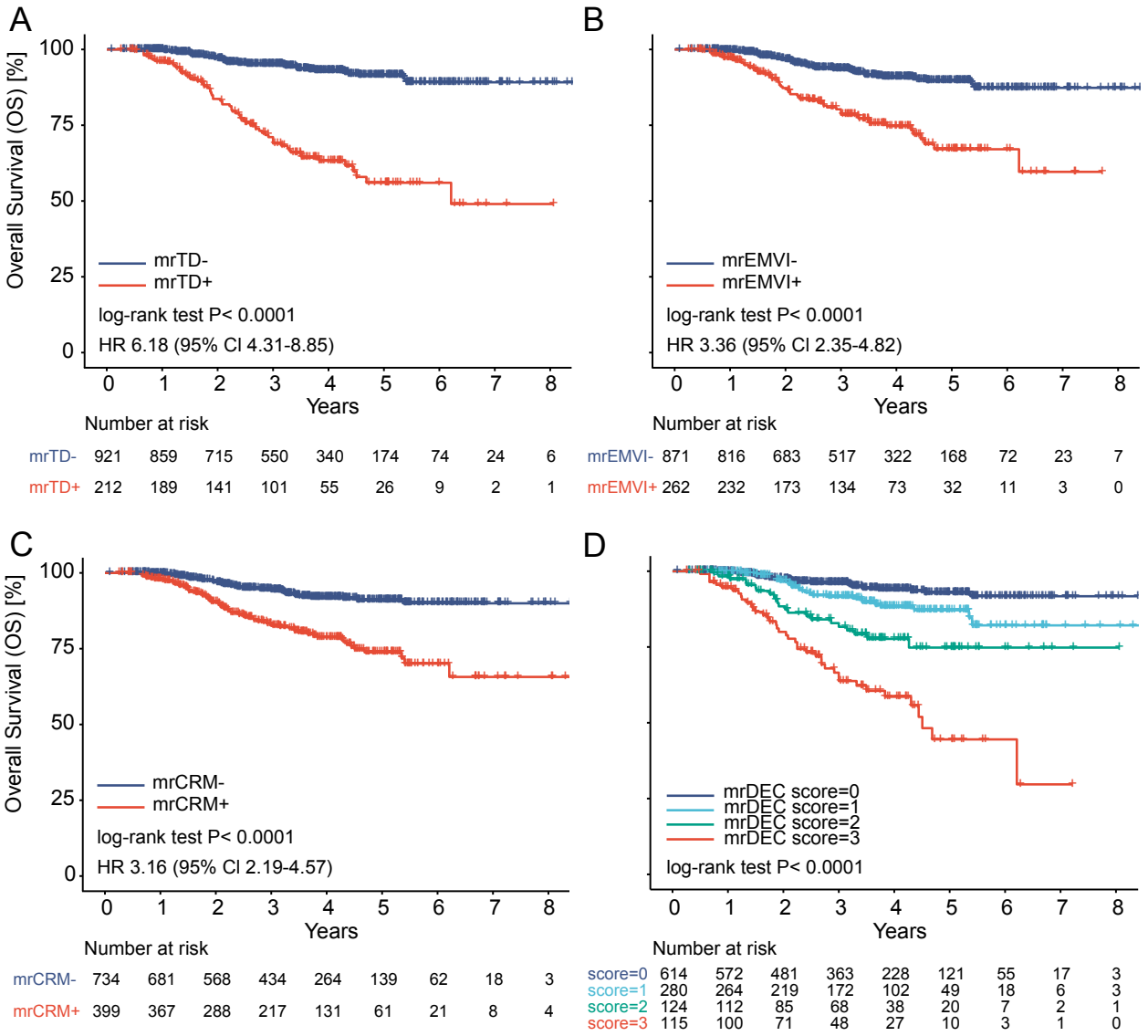

Figure S2. Kaplan-Meier curves for overall survival (OS). Kaplan-Meier survival curves for overall survival according to (A) mrTD status, (B) mrEMVI status, (C) mrCRM status, and (D) mrDEC score. mr, magnetic resonance; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin; HR, hazard ratio.

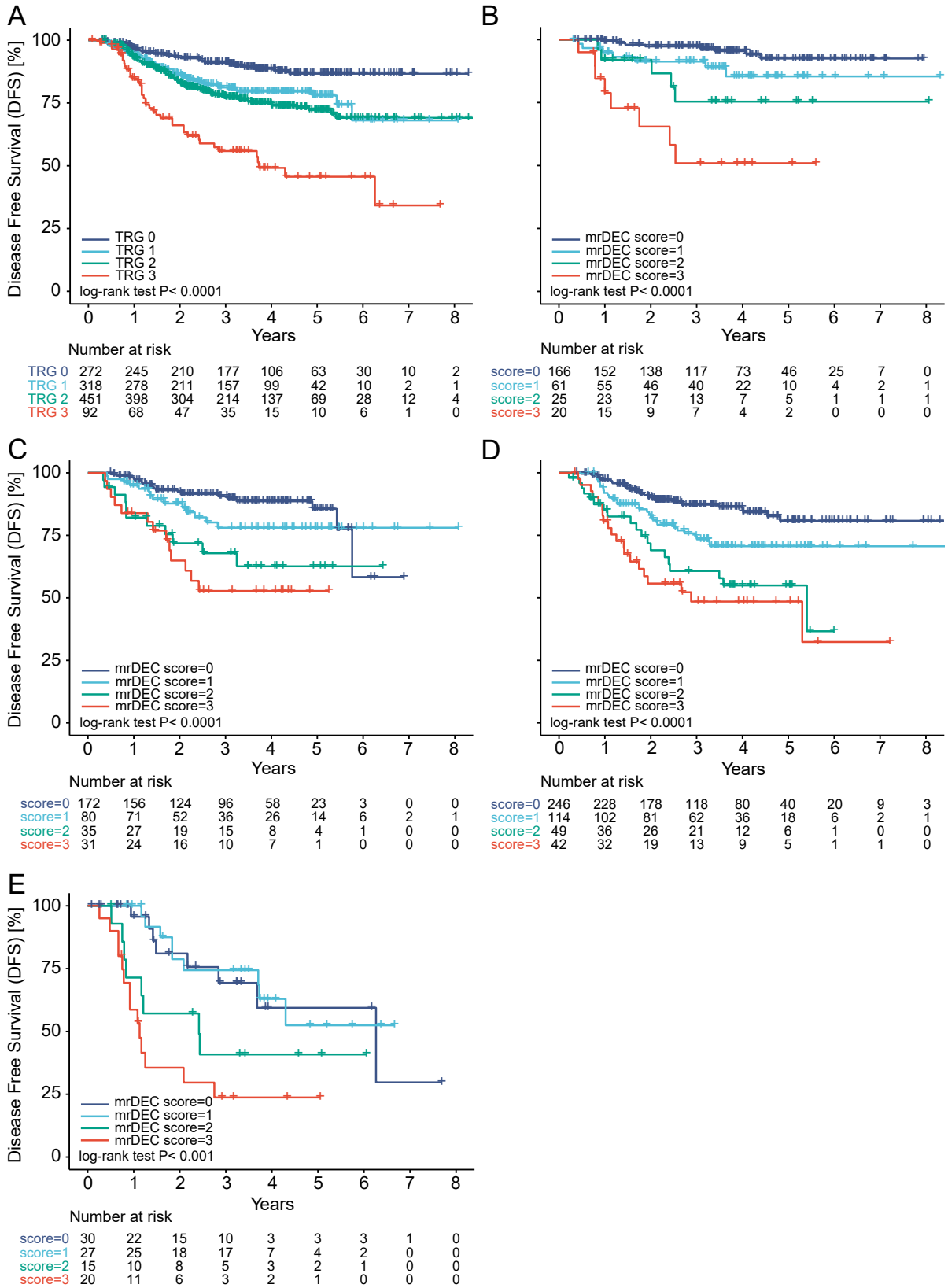

Figure S3. Kaplan-Meier curves for disease-free survival (DFS) according to TRG and mrDEC score. (A) Kaplan-Meier survival curves for disease-free survival according to TRG. Kaplan-Meier survival curves for disease-free survival in patients with (B) TRG 0, (C) TRG 1, (D) TRG 2, and (E) TRG 3 according to mrDEC score. TRG, tumor regression grade.

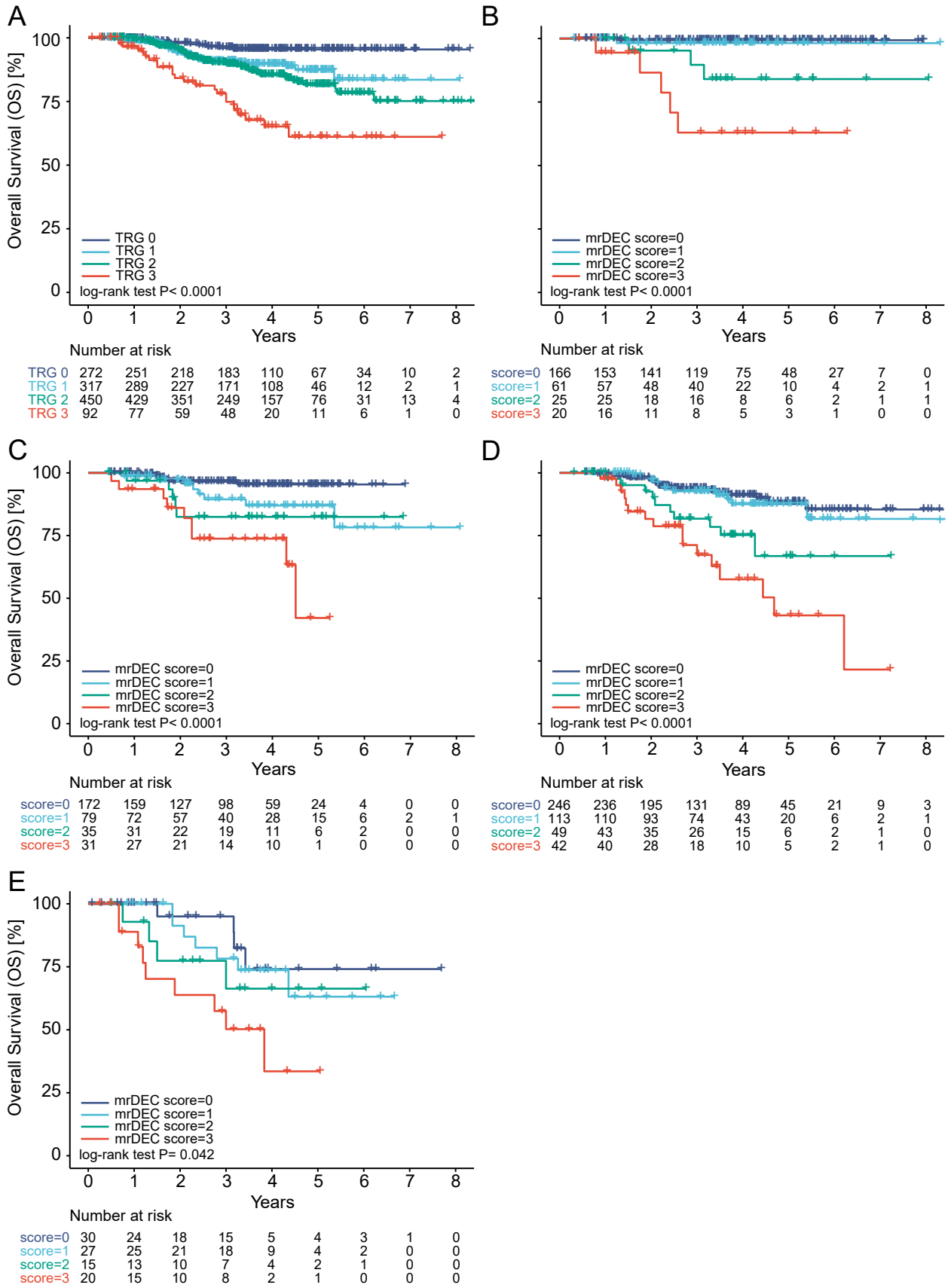

Figure S4. Kaplan-Meier curves for overall survival (OS) according to TRG and mrDEC score. (A) Kaplan-Meier survival curves for overall survival according to TRG. Kaplan-Meier survival curves for overall survival in patients with (B) TRG 0, (C) TRG 1, (D) TRG 2, and (E) TRG 3 according to mrDEC score. TRG, tumor regression grade.

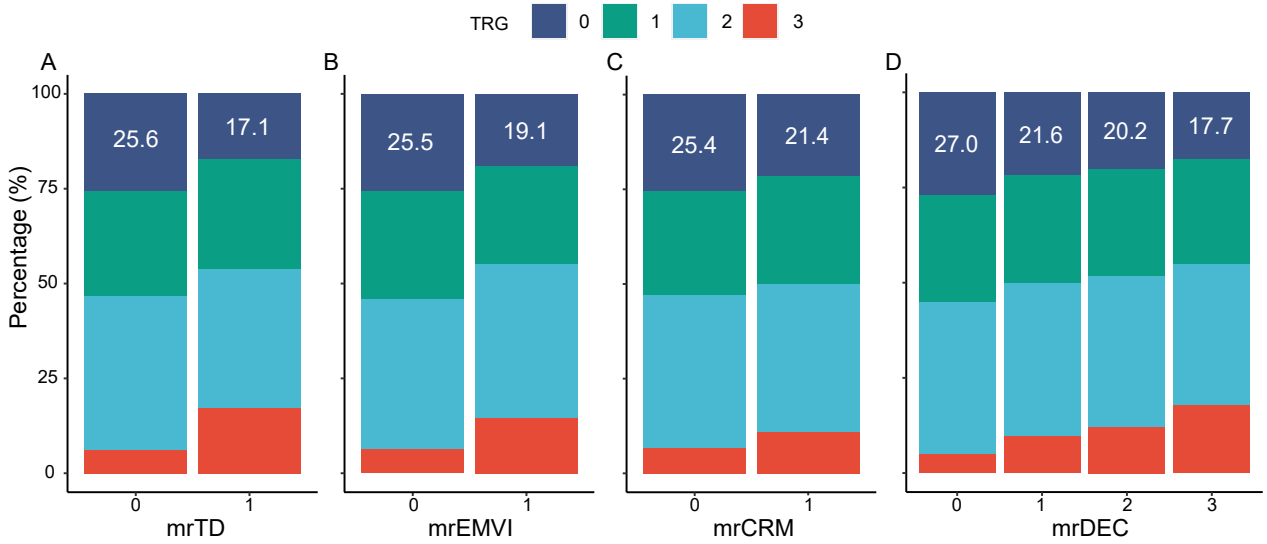

Figure S5. Stacked bar chart of tumor regression grade in Cohort 1. Efficacy analysis of neoadjuvant therapy according to (A) mrTD status, (B) mrEMVI status, (C) mrCRM status, and (D) mrDEC score. TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin; TRG, tumor regression grade.

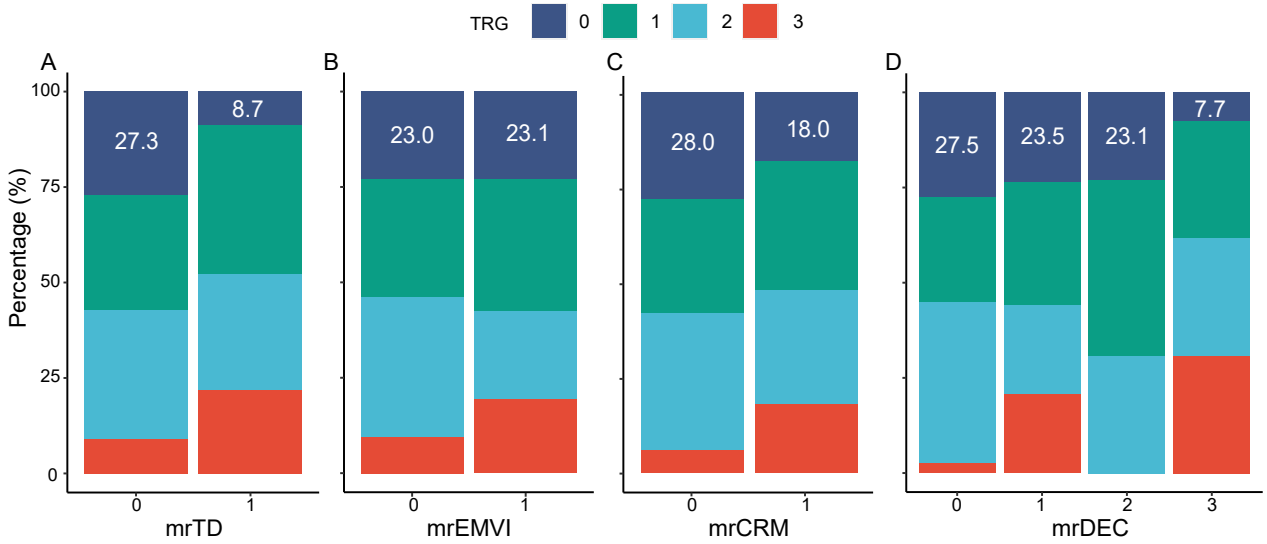

Figure S6. Stacked bar chart of tumor regression grade in Cohort 2. Efficacy analysis of neoadjuvant therapy according to (A) mrTD status, (B) mrEMVI status, (C) mrCRM status, and (D) mrDEC score. TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin; TRG, tumor regression grade.

Table S1. The MRI image acquisition parameters of the multiple centers

Hospital	Scanner	Patients No.	Sequence	TR/TE[a] (ms)	FOV (mm)	Matrix	Slice Thickness (mm)	Slice Gap (mm)	Slices	Flip Angle
Guangdong Provincial People's Hospital	Philips 3.0T (Ingenia)	54	T2WI[b]	4300/141.12	100	464×461	4	5.1	24	90°
			DWI[b]	922.18/65.658	74	108×105	6	7	36	90°
			CE-T1WI[b]	4/1	121	280×278	4	2	80	10°
The Sixth Affiliated Hospital of Sun Yat-sen University	GE 3.0T (OPTIMA)	300+43[c]	T2WI	4300/104	100	288×256	3	6	26	90°
			DWI	4500/92	100	192×192	3	6	20	90°
			CE-T1WI	6/3	90	288×256	2	5	44	12°
Sun Yat-sen University Cancer Center	Philips 3.0T (Achieva)	45	T2WI	2852/90	100	516×510	5	6	32	90°
			DWI	2374/51	70	132×127	5	5·5	36	90°
			CE-T1WI	6/3	90	288×285	6	7	40	10°
	GE 3.0T (DISCOVERY)	105	T2WI	6480·728/81.692	100	382×384	5	6	36	90°
			DWI	4000/56.7	80	128×128	5	6	24	90°
			CE-T1WI	4/2	80	320×140	3	5	40	10°
	GE 1.5T (SIGNA)	90	T2WI	6000/92.184	60	320×224	5	10	24	90°
			DWI	5000/75.6	100	128×128	6	7	25	90°
			CE-T1WI	4/2	83	288×256	2	5	41	11°
	SIEMENS 3.0T (Trio Tim)	237	T2WI	3000/84	75	384×230	5	6	30	90°
			DWI	4000/70	50	128×64	5	6	24	90°
			CE-T1WI	5/2	82	288×211	2	4	44	9°
Shanxi Cancer Hospital	Philips 3.0T (Achieva)	185	T2WI	3000/80	100	300×223	3	3.3	20	90°
			DWI	2750/53	80	124×187	5	5.5	32	90°
			CE-T1WI[d]	623.638/20	115	408×367	6	7.5	32	90°
Yunnan Cancer Hospital	SIEMENS 1.5T (Avanto)	80	T2WI	3200/100	100	288×320	4	4	20	90°
			DWI	4900/84	80	220×220	4	6	24	90°
			CE-T1WI	5/2	75	320×163	6	3	39	10°

	Philips 3.0T (Ingenia)	70+31	T2WI	2100/100	100	400×284	4	4	18	90°
			DWI	3070/62	100	108×129	3	6	40	90°
			CE-T1WI	3/1	90	268×250	5	5	40	10°
Sir Run Run Shaw Hospital of Zhejiang University	GE 3.0T (SIGNA)	+18	T2WI	3200/132	100	320×224	5	6	30	90°
			DWI	5900/66	80	96×130	5	6	30	90°
			CE-T1WI	4/2	90	320×256	4	2	72	12°
Nanfang Hospital of Southern Medical University	Philips 3.0T	+8	T2WI	4000/100	100	316×314	3	3	28	90°
			DWI	2000/60	100	120×118	4	4	28	90°
			CE-T1WI	6/3	100	227×228	6	4	24	10°

Note: Data were *n* or metric value. [a]TR, repetition time; TE, echo time; FOV, field of view. [b]T2WI, T2 weighted imaging; DWI, diffusion weighted imaging; CE-T1WI, contrast enhanced-T1 weighted imaging. [c+] num, indicated the case number in the prospective cohort. [d]STIR sequences.

Table S2. Evaluation criterion of MRI markers in rectal cancer

Imaging features		**Definition and imaging findings**	
mrT stage	T1 or T2	Intact hypointense line surrounding the rectum on MRI	
	T3	Interruption of the hypointense muscularis propria with specular or nodular extension of tumor signal beyond the rectal wall into the mesorectal fat.	
	T4a	Invade the peritoneum or peritoneal reflection	
	T4b	Invade other organs or structures outside the mesorectum	
mrN stage	N0	No suspicious lymph nodes	Suspicious if > 9mm 5-9mm, and 2 malignant characteristics < 5mm, and 3 malignant characteristics Malignant characteristics: indistinct border, heterogeneous signal, and round shape
	N1	1-3 suspicious lymph nodes / no suspicious lymph nodes but tumor deposits	
	N2	⩾3 suspicious lymph nodes	
mrEMVI	Positive	Tumor signal extending within vessel	
	Negative	No involved vessels in vicinity of tumor	
Involved mrCRM		Tumor directly invades the CRM or the margin between the tumor and CRM is ≤ 1 mm (including extramural venous invasion, tumor deposits or irregular lymph nodes)	
mrTD		Irregular nodules within the mesorectum that directly interrupt the course of veins but are discontinuous from the primary tumor.	

Abbreviations: MRI, Magnetic Resonance Imaging; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.

Table S3. Descriptive analysis of tumor characteristics in Cohort 1 stratified by MRI markers

	mrTD negative	mrTD positive	*P*	mrEMVI negative	mrEMVI positive	*P*	mrCRM clear	mrCRM involved	*P*
Age, years			0.152			0.116			0.001
Mean±SD	54.8±11.1	53.6±12.3		54.9±11.2	53.7±1.7		55.4±10.8	53.2±12.1	
Sex			0.165			0.207			0.968
Male	647 (67.5)	143 (62.4)		587 (65.5)	203 (69.8)		505 (66.4)	285 (66.7)	
Female	311 (32.5)	86 (37.6)		309 (34.5)	88 (30.2)		255 (33.6)	142 (33.3)	
CEA level			0.008			0.127			0.550
Normal	580 (60.5)	116 (50.7)		537 (59.9)	159 (54.6)		451 (59.3)	245 (57.4)	
Abnormal	378 (39.5)	113 (49.3)		359 (40.1)	132 (45.4)		309 (40.7)	182 (42.6)	
Location			0.001			0.018			<0.001
Low	481 (50.2)	88 (38.4)		448 (50.0)	121 (41.6)		391 (51.4)	178 (41.7)	
Middle	434 (45.3)	120 (52.4)		406 (45.3)	148 (50.9)		345 (45.4)	209 (48.9)	
High	43 (4.5)	21 (9.2)		42 (4.7)	22 (7.6)		24 (3.2)	40 (9.4)	
cTNM stage			<0.001			<0.001			<0.001
II	182 (19.0)	11 (4.8)		178 (19.9)	15 (5.2)		154 (20.3)	39 (9.1)	
III	776 (81.0)	218 (95.2)		718 (80.1)	276 (94.8)		606 (79.7)	388 (90.9)	
mrT stage			<0.001			<0.001			<0.001
T1-T2	10 (1.0)	0 (0.0)		10 (1.1)	0 (0.0)		10 (1.3)	0 (0.0)	
T3	820 (85.6)	157 (68.6)		771 (86.0)	206 (70.8)		731 (96.2)	246 (57.6)	
T4	128 (13.4)	72 (31.4)		115 (12.8)	85 (29.2)		19 (2.5)	181 (42.4)	
mrN stage			<0.001			<0.001			<0.001
N0	343 (35.8)	5 (2.2)		328 (36.6)	20 (6.9)		290 (38.2)	58 (13.6)	
N1	352 (36.7)	88 (38.4)		333 (37.2)	107 (36.8)		297 (39.1)	143 (33.5)	
N2	263 (27.5)	136 (59.4)		235 (26.2)	164 (56.4)		173 (22.8)	226 (52.9)	

Unless otherwise indicated, data are number of patients and data in parentheses are percentages.

Abbreviation: mr, magnetic resonance; CEA, carcinoembryonic antigen; TNM, tumor-node-metastasis; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.

Table S4. Descriptive analysis of tumor characteristics in Cohort 2 stratified by MRI markers

	mrTD negative	mrTD positive	*P*	mrEMVI negative	mrEMVI positive	*P*	mrCRM clear	mrCRM involved	*P*
Age, years			0.532			0.534			0.089
Mean±SD	56.9±12.3	58.7±11.4		57.8±11.8	56.0±12.9		59.4±10.1	55.3±13.5	
Sex			0.570			0.693			1.000
Male	57 (74.0)	19 (82.6)		55 (74.3)	21 (80.8)		38 (76.0)	38 (76.0)	
Female	20 (26.0)	4 (17.4)		19 (25.7)	5 (19.2)		12 (24.0)	12 (24.0)	
cTNM stage			NA			NA			NA
II	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
III	77 (100)	23 (100)		74 (100)	26 (100)		50 (100)	50 (100)	
mrT stage						0.254			<0.001
T1-T3	61 (79.2)	18 (78.3)	1.000	61 (82.4)	18 (69.2)		50 (100)	29 (58.0)	
T4	16 (20.8)	5 (21.7)		13 (17.6)	8 (30.8)		0 (0.0)	21 (42.0)	
mrN stage			0.002			0.013			0.061
N0	23 (29.9)	0 (0.0)		21 (28.4)	2 (7.7)		16 (32.0)	7 (14.0)	
N1	30 (39.0)	8 (34.8)		30 (40.5)	8 (30.8)		19 (38.0)	19 (38.0)	
N2	24 (31.2)	15 (65.2)		23 (31.1)	16 (61.5)		15 (30.0)	24 (48.0)	

Unless otherwise indicated, data are number of patients and data in parentheses are percentages.
Abbreviation: TNM, tumor-node-metastasis; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.

Table S5. Descriptive analysis of tumor characteristics in Cohort 1 stratified by mrDEC score

	mrDEC score=0	mrDEC score=1	mrDEC score=2	mrDEC score=3	*P*
Age, years					0.025
Mean±SD	55.5±10.7	53.7±11.8	54.1±11.7	52.8±12.3	
Sex					0.434
Male	419 (66.1)	192 (66.7)	98 (72.1)	81 (62.8)	
Female	215 (33.9)	96 (33.3)	38 (27.9)	48 (37.2)	
CEA level					0.161
Normal	386 (60.9)	165 (57.3)	80 (58.8)	65 (50.4)	
Abnormal	248 (39.1)	123 (42.7)	56 (41.2)	64 (49.6)	
Location					<0.001
Low	330 (52.1)	134 (46.5)	62 (45.6)	43 (33.3)	
Middle	283 (44.6)	134 (46.5)	68 (50.0)	69 (53.5)	
High	21 (3.3)	20 (6.9)	6 (4.4)	17 (13.2)	
cTNM stage					<0.001
II	145 (22.9)	38 (13.2)	3 (2.2)	7 (5.4)	
III	489 (77.1)	250 (86.8)	133 (97.8)	122 (94.6)	
mrT stage					<0.001
T1-T2	10 (1.6)	0 (0.0)	0 (0.0)	0 (0.0)	
T3	608 (95.9)	194 (67.4)	110 (80.9)	65 (50.4)	
T4	16 (2.5)	94 (32.6)	26 (19.1)	64 (49.6)	
mrN stage					<0.001
N0	279 (44.0)	57 (19.8)	10 (7.4)	2 (1.6)	
N1	234 (36.9)	116 (40.3)	48 (35.3)	42 (32.6)	
N2	121 (19.1)	115 (39.9)	78 (57.4)	85 (65.9)	

Unless otherwise indicated, data are number of patients and data in parentheses are percentages.

Abbreviation: mr, magnetic resonance; CEA, carcinoembryonic antigen; TNM, tumor-node-metastasis; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.

Table S6. Descriptive analysis of tumor characteristics in Cohort 2 stratified by mrDEC score

	mrDEC score=0	**mrDEC score=1**	**mrDEC score=2**	**mrDEC score=3**	***P***
Age, years					0.796
Mean±SD	58.8±9.8	56.6±13.7	55.5±15.3	56.5±11.0	
Sex					0.492
Male	31 (77.5)	23 (67.6)	11 (84.6)	11 (84.6)	
Female	9 (22.5)	11 (32.4)	2 (15.4)	2 (15.4)	
cTNM stage					NA
II	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
III	40 (100)	34 (100)	13 (100)	13 (100)	
mrT stage					<0.001
T1-T3	40 (100.0)	21 (61.8)	10 (76.9)	8 (61.5)	
T4	0 (0.0)	13 (38.2)	3 (23.1)	5 (38.5)	
mrN stage					0.004
N0	16 (40.0)	5 (14.7)	2 (15.4)	0 (0.0)	
N1	15 (37.5)	16 (47.1)	2 (15.4)	5 (38.5)	
N2	9 (22.5)	13 (38.2)	9 (69.2)	8 (61.5)	

Unless otherwise indicated, data are number of patients and data in parentheses are percentages.
Abbreviation: TNM, tumor-node-metastasis; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.

Table S7. Inter-reader agreement for the assessment of MRI marker status and mrDEC score in 60 patients

	Cohen's kappa[a]			
	mrTD[b]	**mrEMVI**	**mrCRM**	**mrDEC**
Senior radiologists (R5/R6)	0.773	0.651	0.720	0.774
Intermediate radiologists (R3/R4)	0.773	0.408	0.481	0.815
Junior radiologists (R1/R2)	0.721	0.444	0.444	0.692

[a]Linear weighted kappa tests were used except for mrDEC which used squared weighted kappa tests.

[b]All MRI markers (mrTD, mrEMVI, and mrCRM) were assessed for status only, not for staging.

Kappa value: 0.81-1.00, excellent agreement; 0.61-0.80, substantial agreement; 0.41-0.60, moderate agreement; 0.21-0.40, fair agreement; 0-0.20, poor or no agreement.

Abbreviation: R, reader; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.

Table S8. Concordance index of markers for DFS and OS predictions in Cohort 1

	Disease-free survival		Overall survival	
	C-index	**95 CI**	**C-index**	**95 CI**
CEA level	0.55	0.52–0.58	0.56	0.51–0.61
Location	0.53	0.50–0.57	0.54	0.50–0.59
cTNM stage	0.52	0.50–0.54	0.50	0.47–0.54
mrT stage	0.55	0.52–0.58	0.57	0.53–0.66
mrN stage	0.55	0.52–0.59	0.56	0.52–0.61
mrTD status	0.67	0.64–0.70	0.69	0.65–0.74
mrEMVI status	0.62	0.59–0.65	0.63	0.59–0.68
mrCRM status	0.60	0.57–0.64	0.64	0.59–0.68
mrDEC status	0.69	0.66–0.73	0.72	0.69–0.75

Abbreviations: C-index, Concordance index; TD, tumor deposit; EMVI, extramural vascular invasion; CRM, circumferential resection margin.