

Propensity Score Matching Reveals a Survival Paradox in Prognostic Outcomes for Late-Stage II and Early-Stage III Colorectal Cancer Patients

Surendran et al.,

Supplementary Data:

Supplementary Table S1: Patients' profile across missingness for OS and RFS

Variables	Total N(%)	Non-missing N(%)	Missing N(%)	P-value
Miss	1933 (100.0)	1622 (83.9)	311 (16.1)	
Stage_				0.178
IIIA	158 (8.2)	132 (8.1)	26 (8.4)	
IIA	920 (47.6)	784 (48.3)	136 (43.7)	
IIB/C	100 (5.2)	77 (4.7)	23 (7.4)	
IIIB/C	755 (39.1)	629 (38.8)	126 (40.5)	
Sex				0.571
Male	967 (50.0)	816 (50.3)	151 (48.6)	
Female	966 (50.0)	806 (49.7)	160 (51.4)	
Operative urgency				0.101
Emergency/urgent	611 (31.6)	525 (32.4)	86 (27.7)	
Elective	1322 (68.4)	1097 (67.6)	225 (72.3)	
PVD				0.522
No	1845 (95.4)	1546 (95.3)	299 (96.1)	
Yes	88 (4.6)	76 (4.7)	12 (3.9)	
CVA				0.575
No	1810 (93.6)	1521 (93.8)	289 (92.9)	
Yes	123 (6.4)	101 (6.2)	22 (7.1)	
History of smoking				0.932
No	1071 (55.4)	898 (55.4)	173 (55.6)	
Yes	862 (44.6)	724 (44.6)	138 (44.4)	
Current smoker				0.171
No	1800 (93.1)	1516 (93.5)	284 (91.3)	
Yes	133 (6.9)	106 (6.5)	27 (8.7)	
IHD				0.534
No	1484 (76.8)	1241 (76.5)	243 (78.1)	
Yes	449 (23.2)	381 (23.5)	68 (21.9)	
Diabetes				0.692
No	1601 (82.8)	1341 (82.7)	260 (83.6)	
Yes	332 (17.2)	281 (17.3)	51 (16.4)	
Hypertension				0.296
No	991 (51.3)	840 (51.8)	151 (48.6)	
Yes	942 (48.7)	782 (48.2)	160 (51.4)	

Chronic renal failure				<0.001
No	1850 (95.7)	1569 (96.7)	281 (90.4)	
Yes	83 (4.3)	53 (3.3)	30 (9.6)	
MI				0.964
No	1816 (93.9)	1524 (94.0)	292 (93.9)	
Yes	117 (6.1)	98 (6.0)	19 (6.1)	
CHF				0.599
No	1829 (94.6)	1539 (94.9)	290 (94.2)	
Yes	101 (5.2)	83 (5.1)	18 (5.8)	
Steroid use				0.824
No	1854 (95.9)	1555 (95.9)	299 (96.1)	
Yes	79 (4.1)	67 (4.1)	12 (3.9)	
Immunosuppressant use				0.577
No	1880 (97.3)	1579 (97.3)	301 (96.8)	
Yes	53 (2.7)	43 (2.7)	10 (3.2)	
ASA score				<0.001
1	317 (16.4)	288 (17.8)	29 (9.3)	
2	734 (38.0)	632 (39.0)	102 (32.8)	
3	795 (41.1)	631 (38.9)	164 (52.7)	
4	86 (4.4)	70 (4.3)	16 (5.1)	
Surgical entry				0.005
Open	406 (21.0)	361 (22.3)	45 (14.5)	
Laparoscopic	1180 (61.0)	966 (59.6)	214 (68.8)	
Hybrid	140 (7.2)	115 (7.1)	25 (8.0)	
Conversion to Laparoscopic	125 (6.5)	110 (6.8)	15 (4.8)	
Robotic	64 (3.3)	52 (3.2)	12 (3.9)	
Ta-TME	18 (0.9)	18 (1.1)	0 (0.0)	
Procedure type				0.305
Right hemicolectomy	732 (37.9)	609 (37.5)	123 (39.5)	
Extended right hemicolectomy	106 (5.5)	85 (5.2)	21 (6.8)	
Left hemicolectomy	79 (4.1)	65 (4.0)	14 (4.5)	
Sigmoid colectomy	15 (0.8)	12 (0.7)	3 (1.0)	
Total colectomy	30 (1.6)	29 (1.8)	1 (0.3)	
Subtotal colectomy	107 (5.5)	90 (5.5)	17 (5.5)	
Proctocolectomy	5 (0.3)	3 (0.2)	2 (0.6)	
High anterior resection	393 (20.3)	325 (20.0)	68 (21.9)	
Low anterior resection	124 (6.4)	106 (6.5)	18 (5.8)	
Ultra-low anterior resection	205 (10.6)	184 (11.3)	21 (6.8)	
APR	51 (2.6)	43 (2.7)	8 (2.6)	
Hartmann's	51 (2.6)	40 (2.5)	11 (3.5)	
Colo-anal anastomosis	15 (0.8)	13 (0.8)	2 (0.6)	
Transverse colectomy	20 (1.0)	18 (1.1)	2 (0.6)	
Chemotherapy				0.030
No	1161 (60.1)	957 (59.0)	204 (65.6)	

Yes	772 (39.9)	665 (41.0)	107 (34.4)	
Tumour type				0.917
Adenocarcinoma	1655 (85.6)	1389 (85.6)	266 (85.5)	
Adenocarcinoma mucinous	251 (13.0)	211 (13.0)	40 (12.9)	
Adenocarcinoma signet	14 (0.7)	12 (0.7)	2 (0.6)	
No residual	13 (0.7)	10 (0.6)	3 (1.0)	
Lymph node yield				<0.001
<12	340 (17.6)	313 (19.3)	27 (8.7)	
12+	1593 (82.4)	1309 (80.7)	284 (91.3)	
Lymph node ratio				0.138
<0.0825	1392 (72.0)	1157 (71.3)	235 (75.6)	
0.0825-0.25	362 (18.7)	304 (18.7)	58 (18.6)	
0.25-0.5	125 (6.5)	112 (6.9)	13 (4.2)	
0.5-1	54 (2.8)	49 (3.0)	5 (1.6)	
Positive_nodes2				0.677
Negative	1065 (55.1)	897 (55.3)	168 (54.0)	
Positive	868 (44.9)	725 (44.7)	143 (46.0)	
Grade of differentiation				0.106
Well	64 (3.3)	48 (3.0)	16 (5.2)	
Undifferentiated	3 (0.2)	3 (0.2)	0 (0.0)	
Poor	414 (21.4)	357 (22.1)	57 (18.4)	
Moderate	1442 (74.6)	1205 (74.7)	237 (76.5)	
Lymphovascular invasion				0.450
No	1156 (59.8)	976 (60.2)	180 (57.9)	
Yes	777 (40.2)	646 (39.8)	131 (42.1)	
IHC results				0.980
Normal	991 (51.3)	770 (76.5)	221 (76.5)	
Deficient Mismatch Repair Protein	304 (15.7)	236 (23.5)	68 (23.5)	
Length of hospital stay				0.013
<5 days	274 (14.2)	215 (13.3)	59 (19.0)	
5-8 days	668 (34.6)	563 (34.7)	105 (33.9)	
8-12 days	452 (23.4)	396 (24.4)	56 (18.1)	
>12 days	538 (27.8)	448 (27.6)	90 (29.0)	
CEA (ng/ml)				0.970
<2.5	419 (21.7)	356 (38.3)	63 (37.7)	
2.5-5	300 (15.5)	253 (27.2)	47 (28.1)	
5+	377 (19.5)	320 (34.4)	57 (34.1)	
Anastomosis formed				0.602
No	70 (3.6)	60 (16.3)	10 (19.2)	
Yes	349 (18.1)	307 (83.7)	42 (80.8)	
Stoma formed				0.560
No	84 (4.3)	72 (19.6)	12 (23.1)	
Yes	335 (17.3)	295 (80.4)	40 (76.9)	
Neoadjuvant therapy				0.308

No	264 (13.7)	226 (56.4)	38 (63.3)	
Yes	197 (10.2)	175 (43.6)	22 (36.7)	
Rectal cancer				0.049
Fixed	36 (1.9)	31 (8.6)	5 (10.6)	
Mobile	285 (14.7)	259 (71.9)	26 (55.3)	
Tethered	86 (4.4)	70 (19.4)	16 (34.0)	
Radiotherapy				0.328
No	747 (38.6)	657 (98.9)	90 (100.0)	
Yes	7 (0.4)	7 (1.1)	0 (0.0)	
	Mean(SD)	Mean(SD)	Mean(SD)	
Patient age at diagnosis	70 (13.9)	70 (13.9)	71 (14.4)	0.699
BMI kg/m ²	27 (5.6)	26 (5.3)	27 (7.2)	0.143
	Median(IQR)	Median(IQR)	Median(IQR)	
Hospital stay duration	8 (5.0 - 12.0)	8 (5.0 - 12.0)	7 (5.0 - 13.0)	0.012

P-value from Fishers exact test, Linear regression, or quantile regression.

P-values for significant results are shown in boldface fonts.

Abbreviations: peripheral vascular disease, PVD; cerebrovascular accident, CVA; ischaemic heart disease, IHD; myocardial infarction, MI; congestive heart failure, CHF; American Society of Anesthesiologists, ASA; trans-anal total mesorectal excision, Ta-TME; abdomino perineal resection, APR; immunohistochemistry, IHC; carcinoembryonic antigen, CEA; Body Mass Index, BMI; interquartile range, IQR.

Supplementary Table S2: Survival measures and mortality rates across stages

Survival Measures	IIIA	IIA	IIB/C	IIIB/C
Overall survival				
1-year survival (95% CI)	0.984 (0.938-0.996)	0.976 (0.962-0.985)	0.958 (0.876-0.986)	0.944 (0.922-0.960)
3-year survival (95% CI)	0.954 (0.893-0.981)	0.919 (0.895-0.937)	0.791 (0.665-0.874)	0.822 (0.786-0.853)
5-year survival (95% CI)	0.921 (0.846-0.960)	0.845 (0.809-0.875)	0.694 (0.532-0.809)	0.739 (0.694-0.777)
Mortality rate (per 100) (95% CI)	1.93 (1.04-3.59)	3.55 (2.92-4.32)	8.57 (5.53-13.28)	6.45 (5.46-7.62)
Relapse free survival				
1-year survival (95% CI)	0.984 (0.938-0.996)	0.966 (0.950-0.977)	0.945 (0.859-0.979)	0.899 (0.872-0.921)
3-year survival (95% CI)	0.954 (0.891-0.981)	0.909 (0.884-0.929)	0.768 (0.637-0.857)	0.782 (0.744-0.816)
5-year survival (95% CI)	0.906 (0.824-0.950)	0.843 (0.808-0.873)	0.598 (0.421-0.737)	0.730 (0.685-0.769)
Mortality rate (per 100) (95% CI)	1.99 (1.07-3.71)	3.70 (3.04-4.50)	9.33 (6.02-14.46)	7.16 (6.06-8.46)

Abbreviations: Confidence Interval, CI.

The missing weights were considered using Inverse probability weight of missingness (IPW) procedure.

Supplementary Table S3: Assessing the quality of matches

Variable	Before matching			After matching		
	Standardised difference	Matching Threshold	Results	Standardised difference	Matching Threshold	Results
Sex Female	0.0023	<0.05	Balanced	0	<0.05	Balanced,
Age <50	0.0497	<0.05	Balanced	0	<0.05	Balanced,
Age 50-75	-0.003	<0.05	Balanced	0	<0.05	Balanced,
Age >75	-0.0252	<0.05	Balanced	0	<0.05	Balanced,
ASA score 1	0.0146	<0.05	Balanced	0	<0.05	Balanced,
ASA score 2	-0.0334	<0.05	Balanced	0	<0.05	Balanced,
ASA score 3	0.0156	<0.05	Balanced	0	<0.05	Balanced,
ASA score 4	0.0151	<0.05	Balanced	0	<0.05	Balanced,
Tumour site right colon	-0.012	<0.05	Balanced	0	<0.05	Balanced,
Tumour site left colon	0.051	>0.05	Unbalanced	0	<0.05	Balanced,
Tumour site rectum	-0.0422	<0.05	Balanced	0	<0.05	Balanced,
Lymph node yield	0.0631	>0.05	Unbalanced	0	<0.05	Balanced,
Lymphovascular invasion	0.3645	>0.05	Unbalanced	0	<0.05	Balanced,
Diabetes	0.0227	<0.05	Balanced	0	<0.05	Balanced,
IHD	-0.0337	<0.05	Balanced	0	<0.05	Balanced,
History of smoking	-0.0573	<0.05	Balanced	0	<0.05	Balanced,
Hypertension	-0.0376	<0.05	Balanced	0	<0.05	Balanced,
Chemotherapy	0.3616	>0.05	Unbalanced	0	<0.05	Balanced,
Neoadjuvant therapy	-0.0016	<0.05	Balanced	0	<0.05	Balanced,

Abbreviations: American Society of Anesthesiologists, ASA; ischaemic heart disease, IHD.

Supplementary Table S4: Detailed balance table

Detailed balance table showing covariate/category-specific SMDs before and after weighting. Categorical variables are displayed by variable category.

Contrast	Covariate	Before SMD	After SMD	Balance Status
IIA vs IIIA	Sex: Female	0.04287358	0.00000037382361	Balanced, <=0.05
IIA vs IIIA	Sex: Male	-0.04287358	-0.00000037382361	Balanced, <=0.05
IIA vs IIIA	Age group: 1	-0.26658666	0.00000217075728	Balanced, <=0.05
IIA vs IIIA	Age group: 2	-0.41283154	-0.00000913128918	Balanced, <=0.05
IIA vs IIIA	Age group: 3	0.58513852	0.00000852541313	Balanced, <=0.05
IIA vs IIIA	ASA score: 1	-0.31675779	-0.00000495383942	Balanced, <=0.05
IIA vs IIIA	ASA score: 2	-0.06801757	-0.00001961178273	Balanced, <=0.05
IIA vs IIIA	ASA score: 3	0.23821495	-0.00000354024347	Balanced, <=0.05
IIA vs IIIA	ASA score: 4	0.23141515	0.00011836436518	Balanced, <=0.05
IIA vs IIIA	Tumour site group: Left colon	0.10663745	-0.00000786814761	Balanced, <=0.05
IIA vs IIIA	Tumour site group: Rectum	-0.61020924	-0.00000730737068	Balanced, <=0.05
IIA vs IIIA	Tumour site group: Right colon	0.41617293	0.00001474050497	Balanced, <=0.05
IIA vs IIIA	Lymphovascular invasion: No	0.15771455	0.00000798177633	Balanced, <=0.05
IIA vs IIIA	Lymphovascular invasion: Yes	-0.15771455	-0.00000798177633	Balanced, <=0.05
IIA vs IIIA	Operative urgency group: Elective	-0.43836280	0.00003260820499	Balanced, <=0.05
IIA vs IIIA	Operative urgency group: Non-elective	0.43836280	-0.00003260820499	Balanced, <=0.05
IIB/C vs IIIA	Sex: Female	0.14895330	-0.00000214129233	Balanced, <=0.05
IIB/C vs IIIA	Sex: Male	-0.14895330	0.00000214129233	Balanced, <=0.05
IIB/C vs IIIA	Age group: 1	-0.12930666	0.00000140253050	Balanced, <=0.05
IIB/C vs IIIA	Age group: 2	-0.51907623	-0.00000296905535	Balanced, <=0.05
IIB/C vs IIIA	Age group: 3	0.61899059	0.00000225698485	Balanced, <=0.05
IIB/C vs IIIA	ASA score: 1	-0.35457528	-0.00000304201841	Balanced, <=0.05
IIB/C vs IIIA	ASA score: 2	-0.12140431	-0.00000502095924	Balanced, <=0.05
IIB/C vs IIIA	ASA score: 3	0.24573292	-0.00000281581767	Balanced, <=0.05
IIB/C vs IIIA	ASA score: 4	0.35060295	0.00004499756541	Balanced, <=0.05
IIB/C vs IIIA	Tumour site group: Left colon	0.09284111	0.00000010816921	Balanced, <=0.05
IIB/C vs IIIA	Tumour site group: Rectum	-0.82287469	-0.00000565317962	Balanced, <=0.05
IIB/C vs IIIA	Tumour site group: Right colon	0.56283439	0.00000561838993	Balanced, <=0.05
IIB/C vs IIIA	Lymphovascular invasion: No	-0.22761119	-0.00000028808334	Balanced, <=0.05
IIB/C vs IIIA	Lymphovascular invasion: Yes	0.22761119	0.00000028808334	Balanced, <=0.05
IIB/C vs IIIA	Operative urgency group: Elective	-0.71049317	-0.00001442489171	Balanced, <=0.05
IIB/C vs IIIA	Operative urgency group: Non-elective	0.71049317	0.00001442489171	Balanced, <=0.05
IIIB/C vs IIIA	Sex: Female	0.02934710	-0.00000005550613	Balanced, <=0.05

Contrast	Covariate	Before SMD	After SMD	Balance Status
IIIB/C vs IIIA	Sex: Male	-0.02934710	0.00000005550613	Balanced, <=0.05
IIIB/C vs IIIA	Age group: 1	-0.04702545	0.00001493520337	Balanced, <=0.05
IIIB/C vs IIIA	Age group: 2	-0.28322477	0.00000208526060	Balanced, <=0.05
IIIB/C vs IIIA	Age group: 3	0.33149649	-0.00001335507371	Balanced, <=0.05
IIIB/C vs IIIA	ASA score: 1	-0.18022701	-0.00000580138156	Balanced, <=0.05
IIIB/C vs IIIA	ASA score: 2	-0.10432864	0.00000305435243	Balanced, <=0.05
IIIB/C vs IIIA	ASA score: 3	0.18795578	-0.00000358396189	Balanced, <=0.05
IIIB/C vs IIIA	ASA score: 4	0.20100514	0.00002385638082	Balanced, <=0.05
IIIB/C vs IIIA	Tumour site group: Left colon	0.20821968	-0.00000447376106	Balanced, <=0.05
IIIB/C vs IIIA	Tumour site group: Rectum	-0.53102463	-0.00000549999857	Balanced, <=0.05
IIIB/C vs IIIA	Tumour site group: Right colon	0.26239749	0.00000974218172	Balanced, <=0.05
IIIB/C vs IIIA	Lymphovascular invasion: No	-0.72944709	0.00000030492225	Balanced, <=0.05
IIIB/C vs IIIA	Lymphovascular invasion: Yes	0.72944709	-0.00000030492225	Balanced, <=0.05
IIIB/C vs IIIA	Operative urgency group: Elective	-0.54465095	-0.00003609616844	Balanced, <=0.05
IIIB/C vs IIIA	Operative urgency group: Non-elective	0.54465095	0.00003609616844	Balanced, <=0.05

Abbreviations: American Society of Anesthesiologists, ASA.

Supplementary Table S5: ATT estimates for complete case analysis

Outcome and stage comparison	ATET ratio (95% CI)	P-value
Mortality		
(IIA vs IIIA)	1.816 (0.834 - 3.950)	0.133
(IIB/C vs IIIA)	4.870 (1.125 - 21.074)	0.034
(IIIB/C vs IIIA)	3.286 (1.522 - 7.095)	0.002
Surgical complications		
(IIA vs IIIA)	0.785 (0.493 - 1.252)	0.310
(IIB/C vs IIIA)	0.541 (0.181 - 1.616)	0.271
(IIIB/C vs IIIA)	1.115 (0.701 - 1.773)	0.645
Medical complications		
(IIA vs IIIA)	0.847 (0.438 - 1.638)	0.622
(IIB/C vs IIIA)	2.529 (0.449 - 14.231)	0.293
(IIIB/C vs IIIA)	0.965 (0.483 - 1.931)	0.920
Any complications		
(IIA vs IIIA)	0.798 (0.543 - 1.175)	0.254
(IIB/C vs IIIA)	1.344 (0.435 - 4.159)	0.608
(IIIB/C vs IIIA)	1.134 (0.770 - 1.671)	0.523
30-day mortality		
(IIA vs IIIA)	NA	---
(IIB/C vs IIIA)	NA	---
(IIIB/C vs IIIA)	NA	---
Metastases/recurrence		
(IIA vs IIIA)	1.419 (0.669 - 3.013)	0.362
(IIB/C vs IIIA)	5.382 (1.665 - 17.404)	0.005
(IIIB/C vs IIIA)	3.691 (1.812 - 7.519)	<0.001
Overall survival		
(IIA vs IIIA)	1.766 (1.344 - 2.321)	<0.001
(IIB/C vs IIIA)	4.182 (2.447 - 7.147)	<0.001
(IIIB/C vs IIIA)	3.365 (2.177 - 5.203)	<0.001
Relapse-free survival		
(IIA vs IIIA)	1.857 (1.433 - 2.407)	<0.001
(IIB/C vs IIIA)	6.200 (1.789 - 21.478)	0.004
(IIIB/C vs IIIA)	3.645 (2.481 - 5.356)	<0.001

ATET ratio is Relative Risk (RR) for binary outcomes and Hazard Ratio (HR) for survival outcomes.

Supplementary Table S6: ATT estimates IIB/T4aN0 and IIC/T4bN0 vs IIIA

Outcome and stage comparison	ATET ratio (95% CI)	P-value
Mortality		
(IIB/T4aN0 vs IIIA)	5.996 (1.249 - 28.779)	0.025
(IIC/T4bN0 vs IIIA)	2.189 (0.669 - 7.165)	0.195
Surgical complications		
(IIB/T4aN0 vs IIIA)	0.549 (0.174 - 1.730)	0.306
(IIC/T4bN0 vs IIIA)	0.826 (0.342 - 1.993)	0.671
Medical complications		
(IIB/T4aN0 vs IIIA)	2.851 (0.365 - 22.296)	0.318
(IIC/T4bN0 vs IIIA)	0.889 (0.210 - 3.771)	0.874
Any complications		
(IIB/T4aN0 vs IIIA)	1.467 (0.379 - 5.671)	0.579
(IIC/T4bN0 vs IIIA)	0.832 (0.371 - 1.865)	0.655
30-day mortality		
(IIB/T4aN0 vs IIIA)		
(IIC/T4bN0 vs IIIA)		
Metastases/recurrence		
(IIB/T4aN0 vs IIIA)	7.756 (2.562 - 23.477)	<0.001
(IIC/T4bN0 vs IIIA)	2.195 (0.662 - 7.278)	0.199
Overall survival		
(IIB/T4aN0 vs IIIA)	4.757 (3.238 - 6.988)	<0.001
(IIC/T4bN0 vs IIIA)	3.335 (1.837 - 6.053)	<0.001
Relapse-free survival		
(IIB/T4aN0 vs IIIA)	7.816 (2.116 - 28.874)	0.002
(IIC/T4bN0 vs IIIA)	3.873 (2.374 - 6.319)	<0.001

ATET ratio is Relative Risk (RR) for binary outcomes and Hazard Ratio (HR) for survival outcomes.

Supplementary Figure S1: Covariate balance before and after weighting

Dashed vertical lines indicate reference SMD thresholds at ± 0.05 and ± 0.10 ; values closer to zero indicate better balance. Abbreviations: American Society of Anesthesiologists, ASA.

