COLORECTAL SURGERY

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Regional variance in treatment and outcomes of locally invasive (T4) rectal cancer in Australia and New Zealand: analysis of the Bi-National Colorectal Cancer Audit

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Key words
centralized care, locally invasive, pelvic exenteration, rectal cancer, rectal cancer, resection margins.

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Accepted for publication 30 March 2022.

doi: 10.1111/ans.17699

Abstract

Backgrounds: Locally invasive T4 rectal cancer often requires neoadjuvant treatment followed by multi-visceral surgery to achieve a radical resection (R0), and referral to a specialized exenteration quaternary centre is typically recommended. The aim of this study was to explore regional variance in treatment and outcomes of patients with locally advanced rectal cancer in Australia and New Zealand (ANZ).

Methods: Data were collected from the Bi-National Colorectal Cancer Audit (BCCA) database. Rectal cancer patients treated between 2007 and 2019 were divided into six groups based on region (state/country) using patient postcode. A subset analysis of patients with T4 cancer was performed. Primary outcomes were positive circumferential resection margin (CRM+), and positive circumferential and/or distal resection margin (CRM/DRM+).

Results: A total of 9385 patients with rectal cancer were identified, with an overall CRM+ rate of 6.4% and CRM/DRM+ rate of 8.6%. There were 1350 patients with T4 rectal cancer (14.4%). For these patients, CRM+ rate was 18.5%, and CRM/DRM+ rate was 24.1%. Significant regional variation in CRM+ (range 13.4–26.0%; $p = 0.025$) and CRM/DRM+ rates (range 16.1–29.3%; $p = 0.005$) was identified. In addition, regions with higher CRM+ and CRM/DRM+ rates reported lower rates of multi-visceral resections: range 24.3–26.8%, versus 32.6–37.3% for regions with lower CRM+ and CRM/DRM+ rates ($p < 0.0001$).

Conclusion: Positive resection margins and rates of multi-visceral resection vary between the different regions of ANZ. A small subset of patients with T4 rectal cancer are particularly at risk, further supporting the concept of referral to specialized exenteration centres for potentially curative multi-visceral resection.

Introduction

In Australia and New Zealand (ANZ), colorectal cancer (CRC) is diagnosed in over 20 000 people annually, making it the second most prevalent cancer after breast cancer in women and prostate cancer in men.[1,2] CRC is responsible for the most cancer-related deaths after lung cancer.[1–3] In approximately a third of these patients, the tumour is located in the rectum. These patients often require intensive treatment consisting of neoadjuvant (chemo) radiotherapy (nCRT) followed by a rectal resection, an operation associated with high rates of postoperative morbidity and quality of life implications.[4,5] In addition recent advances in neoadjuvant treatment protocols, and attempts at organ preservation, have added to the complexity of rectal cancer care.[6,7]

In case of locally invasive (T4) rectal cancer, with tumour invading into adjacent organs or bony structures, most patients treated with curative intent require a multi-visceral resection or pelvic exenteration (PE) to obtain a microscopically complete radical resection (R0).[8] PE is complex surgery, involving multiple specialties such as colorectal, gynaeoncology, urology, orthopaedics and plastic surgery, and is associated with even higher rates of morbidity and mortality.[9] Centralisation of rectal cancer care in high-volume centres has been shown to improve outcomes in terms of higher rates of R0 resections and lower complication rates, which is especially true for patients requiring PE.[10–12] Therefore,

surgical societies from various countries have set volume limits of minimum numbers of rectal cancer cases that should be performed per hospital per year and have appointed designated centres to perform PE to improve patient outcomes.[13,14]

Currently there are no formalized referral patterns or guidelines for referral to high-volume exenteration centres in ANZ, with limited centralisation in certain metropolitan areas driven informally by local clinicians, representative societies and larger centres. This has resulted in non-formalized established referral patterns to higher-volume centres in each state, territory, and island, with patient referrals made based on the judgement of the treating surgeon and multi-disciplinary team (MDT).

As a result, little is known about the variance in treatment and outcomes for locally advanced rectal cancer between different regions in ANZ.[15,16] Therefore, the aim of the current study was to explore and document this variance using prospectively collected registry data.

Methods

All data were derived from the Bi-National Colorectal Cancer Audit (BCCA), a prospective multi-institutional ANZ clinical quality registry. Since its introduction in 2007, participation in the BCCA has increased yearly and since 2018 it has become mandatory for all accredited colorectal fellowship training centres to enter their patient data.[17] This study was approved by the BCCA Operations Committee and the Central Adelaide Local Health Network Human Research Ethics Committee (HREC/18/CALHN/11924).

Included were rectal cancer patients registered in the BCCA between January 2007 and December 2019 who underwent a rectal resection by means of a high anterior resection (HAR), (ultra)-low anterior resection (LAR or ULAR), abdominoperineal resection (APR), Hartmann's procedure, proctocolectomy, total colectomy, or other rectal resections such as multi-visceral resections. Patients who did not undergo a rectal resection ('watch and wait' or transanal local procedures), and those whose postcodes were missing in the BCCA (and thus whose state/country could not be retrieved) were excluded. The cohort was divided in the following six regions (state/country) based on the patient's postcode: New South Wales (NSW), Victoria (VIC), Queensland (QLD), Western Australia (WA), South Australia (SA), and New Zealand (NZ). Because of insufficient patient numbers for analysis ($n < 200$), patients with Australian Capital Territory (ACT), Tasmania (TAS) and Northern

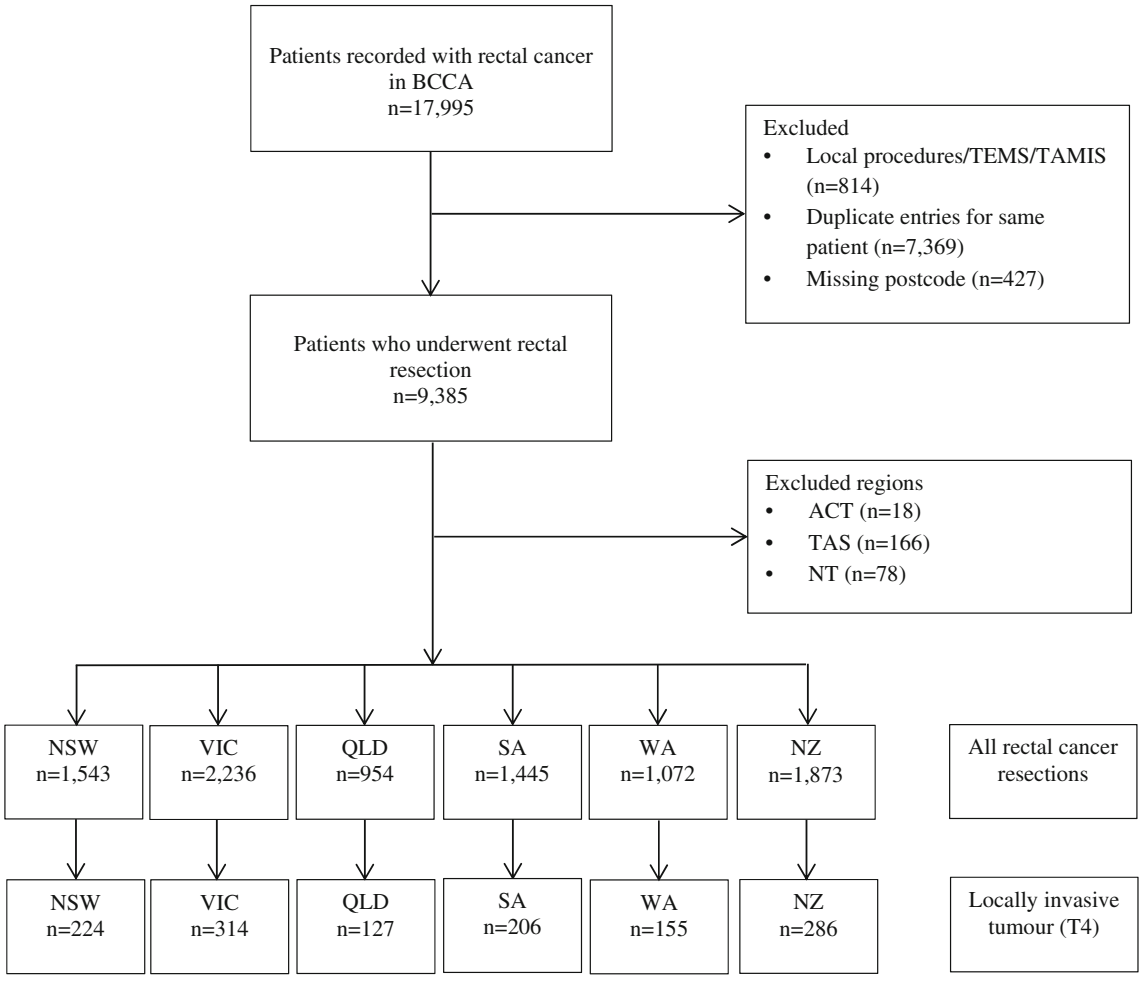

Fig. 1. Flow-chart of patient selection from Bi-National Colorectal Cancer Audit database. Abbreviations: BCCA: Bi-National Colorectal Audit, TEMS: transanal endoscopic microsurgery, TAMIS: transanal minimally invasive surgery, ACT: Australian Capital Territory, TAS: Tasmania, NT: Northern Territories, NSW: New South Wales, VIC: Victoria, QLD: Queensland, SA: South Australia, WA: West Australia, NZ: New Zealand.

Table 1 Characteristics and outcomes of patients treated for locally invasive (T4) rectal cancer in Australia and New Zealand as recorded in the bi-National Colorectal Cancer Audit (BCCA)

Characteristic	No. of patients (%) ($n = 1350$)
Gender (%)	
Male	725 (53.7)
Female	625 (46.3)
Age in years, median (IQR)	65 (20.0)
BMI in kg/m^2, median (IQR)	25.4 (6.9)
Missing	*926*
ASA score (%)	
I/II	822 (64.0)
III/IV/V	462 (36.0)
Missing	*66*
Hospital location (%)	
Urban	1189 (88.1)
Rural	161 (11.9)
Hospital type (%)	
Public	873 (72.9)
Private	324 (27.1)
Missing	*153*
Discussed at MDT (%)	
Yes	876 (84.1)
No	166 (15.9)
Missing	*308*
Preoperative MRI (%)	
Yes	866 (78.4)
No	238 (21.6)
Missing	*246*
Clinical Nodal (cN) stage (%)	
N0	216 (22.9)
N1	299 (31.7)
N2	372 (39.4)
Nx[†]	56 (5.9)
Missing	*407*
Tumour height from anal verge in cm (%)	
Upper rectum >12 cm	144 (13.6)
Middle rectum 8–12 cm	387 (36.7)
Low rectum <8 cm	524 (49.7)
Missing	*295*
Neoadjuvant (chemo)radiotherapy (%)	
Yes	762 (60.0)
No	507 (40.0)
Missing	*81*
Neoadjuvant (chemo)radiotherapy, by tumour height (%)	
Upper rectum (>12 cm; $n = 126$)	
Yes	33 (24.1)
No	104 (75.9)
Missing	*7*
Middle rectum (8–12 cm; $n = 345$)	
Yes	237 (62.2)
No	144 (37.8)
Missing	*6*
Lower rectum (<8 cm; $n = 477$)	
Yes	409 (78.5)
No	112 (21.5)
Missing	*3*
Type of neoadjuvant therapy (for neoadjuvant patients only: $n = 762$) (%)	
Short-course RT	54 (7.5)
Long-course CRT	645 (89.4)
Other	22 (3.1)
Missing	*41*
Operative urgency (%)	
Emergency	63 (4.7)
Urgent	101 (7.5)
Elective	1181 (87.8)
Missing	*5*
Procedure type (%)	
High anterior resection	113 (8.4)
LAR	338 (25.0)
ULAR	377 (27.9)
APR/proctocolectomy	403 (29.9)
Other	119 (8.8)
Multi-visceral resection (%)	
Yes	394 (29.2)
No	956 (70.8)
Approach (%)	
Open	774 (58.2)
Minimally invasive[‡]	555 (41.8)
Missing	*21*
Conversion to open (for minimally invasive cases only: n = 555) (%)	44 (7.9)
Anastomosis formed (%)	
Yes	645 (56.5)
No	496 (43.5)
Missing	*209*
Stoma formed (%)	
Yes	1015 (81.9)
No	160 (12.9)
Already present	64 (5.2)
Missing	*111*
Type of stoma (for stoma patients only: $n = 1079$) (%)	
Loop ileostomy	441 (43.4)
End ileostomy	38 (3.7)
Loop colostomy	56 (5.5)
End colostomy	480 (47.3)
Missing	*64*
Surgical complications (%)	
Yes	421 (31.2)
No	929 (68.8)
Surgical complications specified (%)	
Anastomotic leakage	50 (3.7)
Pelvic collection	85 (6.3)
Superficial wound dehiscence	62 (4.6)
Deep wound dehiscence	23 (1.7)
Wound infection	74 (5.5)
Sepsis	58 (4.3)
Postoperative ileus	141 (10.4)
Small bowel obstruction	20 (1.5)
Urinary retention	41 (3.0)
Ureteric injury	11 (0.8)
Postoperative haemorrhage	17 (1.3)
Return to theatre	119 (8.8)
Other surgical complications	90 (6.7)
Medical complications (%)	
Yes	198 (14.7)
No	1152 (85.3)
Medical complications specified (%)	
DVT/PE	20 (1.5)
Chest infection	56 (4.1)
Cardiac	49 (3.6)
Other medical complications	117 (8.7)
In-hospital mortality (%)	
Yes	16 (1.2)
No	1334 (98.9)
Hospital stay in days, median (IQR)	10.0 (9.0)
Missing	*279*
30-day readmission (%)	
Yes	115 (8.5)
No	1235 (91.5)

Table 1 Continued

Characteristic	No. of patients (%) ($n = 1350$)
Pathological nodal (pN) stage (%)	
N0	590 (45.1)
N1	401 (30.6)
N2	265 (20.2)
Nx[§]	53 (4.0)
Missing	*41*
Number of lymph nodes harvested, median (range)	16 (0–85)
Number of tumour positive lymph nodes (for N+ patients only), median (range)	3 (1–41)
Tumour regression grade (for neoadjuvant cases only ($n = 762$) (%)	
Complete (grade 0)	60 (11.4)
Moderate (grade 1)	91 (17.4)
Minimal (grade 2)	234 (44.7)
Poor (grade 3)	139 (26.5)
Missing	*238*
DRM (%)	
Positive	46 (4.4)
Negative	1004 (95.6)
Missing	*300*
CRM (%)	
Positive	205 (18.5)
Negative	906 (81.5)
Missing	*239*
CRM and/or DRM positive (%)	
Yes	230 (24.1)
No	725 (75.9)
Missing	*395*
Adjuvant chemotherapy (%)	
Yes	708 (52.4)
No	642 (47.6)

Abbreviations: APR, abdominoperineal resection; ASA, American Society of Anesthesiologists; BMI, body mass index; CRM, circumferential resection margin; CRT; chemo-radiotherapy; DVT/PE, deep venous thrombosis/pulmonary embolism; DRM, distant resection margin; IQR, interquartile range; LAR, low anterior resection; MDT, multidisciplinary team; MRI, magnetic resonance imaging; RT, radiotherapy; ULAR, ultralow anterior resection.

[†]Clinical nodal stage could not be assessed.

[‡]Laparoscopic/transanal total mesorectal excision (taTME)/robotic/hybrid procedures.

[§]Pathological nodal stage could not be assessed.

Territories (NT) postcodes could not be included in the analysis by region. Australian and New Zealand Bureaus of Statistics were consulted for accurate population numbers of the different regions.[18,19] A hospital was identified as 'urban' if it was located in a city with a population exceeding 100 000 inhabitants. AJCC tumour regression grade (TRG) after neoadjuvant treatment was defined as follows: grade 0, no residual tumour cells in the resected specimen; grade 1, single cells or small groups of cells; grade 2, residual cancer with desmoplastic response; and grade 3, minimal tumour response.[20,21] A multi-visceral resection was defined by the removal one or more of the following organs: uterus, prostate, bladder, kidney, seminal vesicles, vaginal wall, ureter, pelvic sidewall and/or bony pelvis. T4 rectal cancer was defined as a clinical (preoperative) and/or pathological (postoperative) T4 stage, or patients who underwent a multi-visceral resection due to tumour invasion.

The primary outcomes were positive circumferential resection margin (CRM positivity) and circumferential and distal resection margin positivity combined (CRM/DRM positivity), both defined as a tumour resection margin of ≤1 mm. Secondary outcome was multi-visceral resection.

Statistical analysis was performed for the complete rectal cancer cohort, with a further *a priori* planned subset analysis for patients with locally invasive (T4) rectal cancer. Continuous parameters are presented as median with range as they were not normally distributed (Shapiro–Wilk test), and categorical outcomes as frequency with percentage. Univariate analyses to compare the six regions were performed using the analysis of variance (ANOVA) for continuous variables and the Chi-square test for categorical variables. A statistically significant value was defined as ≤0.05. Statistical analyses were conducted using IBM SPSS version 26 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 8.0.2 (GraphPad Software Inc., San Diego, CA, USA).

Results

Figure 1 shows the flow-diagram of patient selection from the BCCA. After removing duplicate entries and applying the exclusion criteria, a total of 9385 rectal cancer patients were identified: NSW $n = 1543$, VIC $n = 2236$, QLD $n = 954$, WA $n = 1072$, SA $n = 1445$, NZ $n = 1873$. Patient demographics and treatment outcomes for the complete rectal cancer cohort are presented in Supplementary Tables A and B. Taking into account the different population sizes, SA registered most rectal cancer patients in the BCCA with 82:100000 inhabitants. NSW (19:100000) and QLD (18:100000) registered the least ($p < 0.0001$). Overall, CRM was positive in 487 (6.4%) patients. Higher CRM positivity was reported in QLD (8.4%) and SA (9.2%) compared to NZ (6.4%), NSW (5.3%), WA (5.1%) and VIC (4.9%) ($p < 0.0001$). CRM/DRM was positive in 568 (8.6%) patients in ANZ, with higher rates in QLD (9.2%) and SA (11.1%) compared to NZ (7.5%), NSW (7.2%) and VIC (6.0%) ($p = 0.005$).

Table 1 presents demographics and treatment characteristics for ANZ patients with T4 tumours ($n = 1350$, 14.4% of all rectal cancers). The majority had low rectal tumours <8 cm from the anal verge or mid-rectal tumours between 8 and 12 cm (49.7% and 36.7%, respectively). More than two third of the patients had clinical nodal involvement (cN1/cN2). Most received neoadjuvant therapy (60%): 78.5% of those with a tumour in the lower rectum, 62.2% and 24.1% with tumours in the middle and upper rectum, respectively. Most received long-course nCRT (89.4%). APR/proctocolectomy was performed most frequently (29.9%), followed by a ULAR and LAR (27.9% and 25%, respectively). Surgical complications and medical complications occurred in 31.2% and 14.7%, respectively with postoperative ileus (10.4%), return to theatre (8.8%) and anastomotic leakage (7.8%) occurring most frequently. Thirty-day readmission rate was 8.5% and in-hospital mortality was 1.2%. CRM was positive in 18.5%, and CRM/DRM was positive in 24.1%.

Table 2 shows outcomes by region for patients with T4 tumours. There were differences in CRM positivity reported in QLD (26%) and SA (24.2%) compared to VIC (17.5%), WA (17.2%), NSW (15.1%) and NZ (13.4%) ($p = 0.025$). Positive CRM/DRM margins were also higher in QLD (29.1%) and SA (29.3%) than in VIC

Table 2 Characteristics and outcomes of patients treated for locally invasive (T4) rectal cancer by region in Australia and New Zealand as recorded in the Bi-National Colorectal Cancer Audit (BCCA)

Characteristic	NSW ($n = 224$)	VIC ($n = 314$)	QLD ($n = 127$)	SA ($n = 206$)	WA ($n = 155$)	NZ ($n = 286$)	*p*-value
Gender (%)							
Male	126 (56.3)	166 (52.9)	70 (55.1)	113 (54.9)	85 (54.8)	151 (52.8)	0.97
Female	98 (43.8)	148 (47.1)	57 (44.9)	93 (45.1)	70 (45.2)	135 (47.2)	
Age in years, median (IQR)	69 (21.2)	63 (22.5)	66 (18.7)	65 (17.9)	66 (19.5)	66 (18.1)	0.087
BMI in kg/m^2, median (IQR)	25.6 (5.9)	25.5 (6.7)	25.3 (8.1)	24.8 (7.1)	*	25.0 (7.4)	0.960
Missing	*154*	*106*	*68*	*192*		*224*	
ASA score (%)							
I/II	142 (67.9)	204 (66.4)	58 (47.2)	117 (57.6)	82 (68.9)	192 (67.4)	0.0003
III/IV/V	67 (32.1)	103 (33.6)	65 (52.8)	86 (42.4)	37 (31.1)	93 (32.6)	
Missing	*15*	*7*	*4*	*3*	*36*	*1*	
Hospital location (%)							
Urban	189 (84.4)	275 (87.6)	114 (89.8)	206 (100)	*	219 (76.6)	<0.0001
Rural	35 (15.6)	39 (12.4)	13 (10.2)	0		67 (23.4)	
Hospital type (%)							
Public	149 (68.0)	195 (63.3)	88 (69.3)	146 (70.9)	*	267 (93.4)	<0.0001
Private	70 (32.0)	113 (36.7)	39 (30.7)	60 (29.1)		19 (6.6)	
Missing	*5*	*6*	*0*	*0*		*0*	
Discussed at MDT (%)							0.0012
Yes	157 (80.9)	239 (78.4)	92 (84.4)	124 (89.9)	*	232 (89.6)	
No	37 (19.1)	66 (21.6)	17 (15.6)	14 (10.1)		27 (10.4)	
Missing	*30*	*9*	*18*	*68*		*27*	
Preoperative MRI (%)							<0.0001
Yes	139 (65.6)	246 (80.7)	87 (73.1)	123 (78.8)	*	238 (87.2)	
No	73 (34.4)	59 (19.3)	32 (26.9)	33 (21.2)		35 (12.8)	
Missing	*12*	*9*	*8*	*50*		*13*	
Clinical Nodal (cN) stage (%)							0.014
N0	35 (22.3)	64 (25.2)	27 (30.0)	20 (15.9)	12 (24.5)	54 (22.2)	
N1	55 (35.0)	89 (35.0)	24 (26.7)	36 (28.6)	13 (26.5)	75 (30.9)	
N2	56 (35.7)	87 (34.3)	34 (37.8)	58 (46.0)	24 (49.0)	102 (42.0)	
Nx[†]	11 (7.0)	14 (5.5)	5 (5.6)	12 (9.5)	0	12 (4.9)	
Missing	*67*	*60*	*37*	*80*	*106*	*43*	
Tumour height from anal verge in cm (%)							
Upper rectum >12 cm	36 (18.4)	41 (14.1)	16 (14.8)	15 (10.9)	13 (22.4)	19 (8.0)	0.165
Middle rectum 8–12 cm	75 (38.3)	98 (33.7)	31 (28.7)	53 (38.7)	23 (39.7)	99 (41.6)	
Low rectum <8 cm	85 (43.4)	152 (52.2)	61 (56.5)	69 (50.4)	22 (37.9)	120 (50.4)	
Missing	*28*	*23*	*19*	*69*	*97*	*48*	
Neoadjuvant (chemo)radiotherapy (%)							
Yes	124 (57.1)	192 (63.2)	67 (52.8)	122 (59.2)	44 (47.8)	186 (65.3)	0.018
No	93 (42.9)	112 (36.8)	60 (47.2)	84 (40.8)	48 (52.2)	99 (34.7)	
Missing	*7*	*10*	*0*	*0*	*63*	*1*	
Neoadjuvant (chemo)radiotherapy, by tumour height (%)							
Upper rectum (>12 cm)							0.078
Yes	5 (15.2)	9 (22.0)	5 (31.2)	1 (6.7)	4 (44.4)	8 (42.1)	
No	28 (84.8)	32 (78.0)	11 (68.8)	14 (93.3)	5 (55.6)	11 (57.9)	
Missing	*3*	*0*	*0*	*0*	*4*	*0*	
Middle rectum (8–12 cm)							
Yes	43 (57.3)	58 (61.0)	14 (45.2)	34 (64.1)	18 (85.7)	64 (65.3)	0.075
No	32 (42.7)	37 (39.0)	17 (54.8)	19 (35.9)	3 (14.3)	34 (34.7)	
Missing	*0*	*3*	*0*	*0*	*2*	*1*	
Lower rectum (<8 cm)							
Yes	66 (78.6)	115 (76.2)	38 (62.3)	58 (84.1)	19 (90.5)	99 (82.5)	0.016
No	18 (21.4)	36 (23.8)	23 (37.7)	11 (15.9)	2 (9.5)	21 (17.5)	
Missing	*1*	*1*	*0*	*0*	*1*	*0*	
Type of neoadjuvant therapy (for neoadjuvant patients only) (%)							
Short-course RT	6 (4.9)	9 (4.7)	9 (13.4)	11 (9.0)	*	18 (9.7)	0.024
Long-course CRT	115 (94.3)	179 (93.7)	56 (83.6)	103 (84.4)		162 (87.1)	
Other	1 (0.8)	3 (1.6)	2 (3.0)	8 (6.6)		6 (3.2)	
Missing	*2*	*1*	*0*	*0*		*0*	
Operative urgency (%)							
Emergency	13 (5.8)	15 (4.8)	5 (4.0)	16 (7.8)	1 (0.6)	11 (3.8)	0.041
Urgent	18 (8.1)	24 (7.6)	12 (9.7)	17 (8.3)	4 (2.6)	21 (7.3)	
Elective	192 (86.1)	275 (87.6)	107 (86.3)	172 (83.9)	150 (96.8)	254 (88.8)	
Missing	*1*	*0*	*3*	*1*	*0*	*0*	

Table 2 Continued

Characteristic	NSW ($n = 224$)	VIC ($n = 314$)	QLD ($n = 127$)	SA ($n = 206$)	WA ($n = 155$)	NZ ($n = 286$)	*p*-value
Procedure type (%)							
High anterior resection	15 (6.7)	17 (5.4)	1 (0.8)	12 (5.8)	48 (31.0)	19 (6.6)	<0.0001
LAR	60 (26.8)	63 (20.1)	31 (24.4)	67 (32.5)	34 (21.9)	74 (25.9)	
ULAR	63 (28.1)	112 (35.7)	36 (28.3)	42 (20.4)	47 (30.3)	71 (24.8)	
APR/proctocolectomy	64 (28.6)	99 (31.5)	47 (37.0)	60 (29.1)	18 (11.6)	98 (34.3)	
Other	22 (9.8)	23 (7.3)	12 (9.5)	25 (12.2)	8 (5.2)	24 (8.3)	
Multi-visceral resection (%)							
Yes	73 (32.6)	117 (37.3)	34 (26.8)	50 (24.3)	*	103 (36.0)	<0.0001
No	151 (67.4)	197 (62.7)	93 (73.2)	156 (75.7)		183 (64.0)	
Approach (%)							
Open	94 (42.2)	171 (54.6)	45 (36.0)	159 (77.9)	85 (55.2)	195 (71.7)	0.011
Minimally invasive[‡]	129 (57.8)	142 (45.4)	80 (64.0)	45 (22.1)	69 44.8)	77 (28.3)	
Missing	*1*	*1*	*2*	*2*	*1*	*14*	
Conversion to open (for minimally invasive cases only) (%)	8 (6.2)	9 (6.3)	8 (10.0)	8 (17.8)	6 (8.70	2 (2.6)	0.111
Anastomosis formed (%)							
Yes	107 (53.2)	165 (54.5)	50 (48.1)	63 (48.1)	*	117 (49.2)	0.570
No	94 (46.8)	138 (45.5)	54 (51.9)	68 (51.9)		121 (50.8)	
Missing	*23*	*11*	*23*	*75*		*48*	
Stoma formed (%)							
Yes	160 (71.7)	247 (79.4)	99 (79.2)	178 (86.4)	*	225 (86.5)	<0.0001
No	51 (22.9)	47 (15.1)	16 (12.8)	25 (12.1)		14 (5.4)	
Already present	12 (5.4)	17 (5.5)	10 (8.0)	3 (1.5)		21 (8.1)	
Missing	*1*	*3*	*2*	*0*		*26*	
Type of stoma (for stoma patients only) (%)							
Loop ileostomy	63 (39.4)	111 (44.9)	36 (36.4)	70 (39.3)	*	99 (44.0)	0.425
End ileostomy	7 (4.4)	10 (4.0)	2 (2.0)	8 (4.5)		7 (3.1)	
Loop colostomy	10 (6.3)	13 (5.3)	10 (10.1)	13 (7.3)		6 (2.7)	
End colostomy	80 (50.0)	113 (45.7)	51 (51.5)	87 (48.9)		113 (50.2)	
Surgical complications (%)							0.807
Yes	72 (32.1)	103 (32.8)	42 (33.1)	72 (35.0)	*	105 (36.7)	
No	152 (67.9)	211 (67.2)	85 (66.9)	134 (65.0)		181 (63.3)	
Surgical complications specified (%)							
Anastomotic leakage	9 (4.0)	11 (3.5)	5 (3.9)	4 (1.9)	*	14 (4.9)	
Pelvic collection	24 (10.7)	16 (5.1)	8 (6.3)	18 (8.7)		14 (4.9)	
Superficial wound dehiscence	12 (5.4)	18 (5.7)	5 (3.9)	9 (4.4)		13 (4.5)	
Deep wound dehiscence	6 (2.7)	4 (1.3)	2 (1.6)	6 (2.9)		5 (1.7)	
Wound infection	16 (7.1)	20 (6.4)	6 (4.7)	11 (5.3)		18 (6.3)	
Sepsis	10 (4.5)	18 (5.7)	6 (4.7)	9 (4.4)		12 (4.2)	
Postoperative ileus	34 (15.2)	35 (11.1)	14 (11.0)	24 (11.7)		27 (9.4)	
Small bowel obstruction	5 (2.2)	5 (1.6)	4 (3.1)	2 (1.0)		2 (0.7)	
Urinary retention	7 (3.1)	10 (3.2)	6 (4.7)	7 (3.4)		10 (3.5)	
Ureteric injury	3 (1.3)	1 (0.3)	2 (1.6)	3 (1.5)		1 (0.3)	
Postoperative haemorrhage	3 (1.3)	7 (2.2)	1 (0.8)	3 (1.5)		3 (1.0)	
Return to theatre	18 (8.0)	38 (12.1)	14 (11.0)	18 (8.7)		20 (7.0)	
Other surgical complications	13 (5.8)	17 (5.4)	12 (9.4)	23 (11.2)		19 (6.6)	
Medical complications (%)							
Yes	34 (15.2)	53 (16.9)	17 (13.4)	43 (20.9)	*	43 (15.0)	0.339
No	190 (84.8)	261 (83.1)	110 (86.6)	163 (79.1)		243 (85.0)	
Medical complications specified (%)							
DVT/PE	6 (2.7)	4 (1.3)	3 (2.4)	4 (1.9)	*	2 (0.7)	
Chest infection	7 (3.1)	14 (4.5)	5 (3.9)	12 (5.8)		16 (5.6)	
Cardiac	7 (3.1)	16 (5.1)	3 (2.4)	11 (5.3)		10 (3.5)	
Other medical complications	13 (5.8)	17 (5.4)	12 (9.4)	23 (11.2)		19 (6.6)	
In-hospital mortality (%)							
Yes	3 (1.3)	3 (1.0)	2 (1.6)	2 (1.0)	0	6 (2.1)	0.52
No	221 (98.7)	311 (99.0)	125 (98.4)	204 (99.0)	155 (100)	280 (97.9)	
Hospital stay in days, median (IQR)	11.0 (11.0)	11.0 (12.0)	9.0 (8.0)	10.0 (9.0)	*	9.0 (6.5)	0.199
Missing	*34*	*36*	*6*	*24*		*26*	
30-day readmission (%)							
Yes	13 (5.8)	30 (9.6)	14 (11.0)	11 (5.3)	*	45 (15.7)	0.0004
No	211 (94.2)	284 (90.4)	113 (89.0)	195 (94.7)		241 (84.3)	
Pathological nodal (pN) stage (%)							
N0	100 (47.2)	139 (45.3)	64 (51.6)	79 (39.7)	58 (37.4)	136 (49.5)	0.004
N1	73 (34.4)	98 (31.9)	34 (27.4)	62 (31.2)	47 (30.3)	75 (27.3)	
N2	36 (17.0)	54 (17.6)	21 (16.9)	47 (23.6)	49 (31.6)	52 (18.9)	
Nx[§]	3 (1.4)	16 (5.2)	5 (4.0)	11 (5.5)	1 (0.6)	12 (4.4)	
Missing	*12*	*7*	*3*	*7*	*0*	*11*	

Table 2 Continued

Characteristic	NSW ($n = 224$)	VIC ($n = 314$)	QLD ($n = 127$)	SA ($n = 206$)	WA ($n = 155$)	NZ ($n = 286$)	*p*-value
Number of lymph nodes harvested, median (range)	16 (0–85)	16 (0–54)	18 (0–51)	14 (0–50)	17 (0–84)	16 (0–42)	0.001
Number of tumour positive lymph nodes (for N+ patients only), median (range)	3 (1–41)	3 (1–28)	3 (1–29)	3 (1–28)	3 (1–28)	3 (1–24)	0.005
Tumour regression grade (for neoadjuvant cases only (%)							
Complete (grade 0)	7 (7.7)	16 (12.8)	10 (21.2)	7 (13.2)	4 (9.8	13 (8.6)	0.104
Moderate (grade 1)	17 (18.7)	20 (16.0)	11 (23.4)	12 (22.6)	7 (17.1)	21 (13.8)	
Minimal (grade 2)	43 (47.2)	59 (47.2)	13 (27.7)	16 (30.2)	24 (58.5)	77 (50.6)	
Poor (grade 3)	24 (26.4)	30 (24.0)	13 (27.7)	18 (34.0)	6 (14.6)	41 (27.0)	
Missing	*33*	*67*	*20*	*69*	*3*	*34*	
DRM (%)							
Positive	10 (5.2)	6 (2.1)	9 (7.8)	12 (6.7)	*	7 (3.0)	0.029
Negative	181 (94.8)	285 (97.9)	106 (92.2)	167 (93.3)		228 (97.0)	
Missing	*33*	*23*	*12*	*27*		*51*	
CRM (%)							
Positive	27 (15.1)	47 (17.5)	27 (26.0)	36 (24.2)	26 (17.2)	31 (13.4)	0.025
Negative	152 (84.9)	221 (82.5)	77 (74.0)	113 (75.8)	125 (82.8)	201 (86.6)	
Missing	*45*	*46*	*23*	*57*	*4*	*54*	
CRM and/or DRM positive (%)							
Yes	33 (18.5)	50 (18.7)	30 (29.1)	43 (29.3)	*	36 (16.1)	0.005
No	145 (81.5)	218 (81.3)	73 (70.9)	104 (70.7)		188 (83.9)	
Missing	*46*	*46*	*24*	*59*		*62*	
Adjuvant chemotherapy (%)							
Yes	113 (50.4)	156 (49.7)	63 (49.6)	140 (68.0)	72 (46.5)	137 (47.9)	<0.0001
No	111 (49.6)	158 (50.3)	64 (50.4)	66 (32.0)	83 (53.5)	149 (52.1)	

Abbreviations: ASA, American Society of Anesthesiologists; APR, abdominoperineal resection; BMI, body mass index; CRM, circumferential resection margin; CRT, chemo-radiotherapy; DRM, distant resection margin; DVT/PE, deep venous thrombosis/pulmonary embolism; IQR, interquartile range; LAR, low anterior resection; MDT, multidisciplinary team; MRI, magnetic resonance imaging; NSW, New South Wales; RT, radiotherapy; ULAR, ultralow anterior resection; VIC, Victoria; QLD, Queensland; SA, South Australia; WA, Western Australia; NZ, New Zealand.

†Clinical nodal stage could not be assessed.

‡Laparoscopic/Transanal total mesorectal excision (taTME)/robotic/hybrid procedures.

§Pathological nodal stage could not be assessed.

*Insufficient data.

(18.7%), NSW (18.5%) and NZ (16.1%) ($p = 0.005$). Rates of multi-visceral resections were different between regions as well with lower rates in QLD (26.8%) and SA (24.3%) than in VIC (37.3%), NSW (32.6%) and NZ (36%) ($p < 0.0001$).

Discussion

This ANZ population study based on BCCA data revealed an overall CRM positivity rate of 6.4% and a CRM/DRM positivity rate of 8.6% after rectal cancer surgery. In patients with T4 tumours, CRM positivity rate was 18.5% and CRM/DRM positivity was 24.1%, both with significant variability between regions (13.4%–26.0% and 16.1%–29.3%, respectively). There also appeared to be correlation between margin positivity rates and the percentage of patients who underwent multi-visceral resections, with regions documenting lower rates of multi-visceral resection, having higher tumour positive margin rates.

Positive CRM is an important prognostic factor for rectal cancer recurrence and of poor survival.[22] The overall CRM positivity rate of 6.4% for all rectal cancers in the current study is slightly lower than reported previously, ranging between 8% and 17%.[16,22–24] Specifically compared to other national audits, the Dutch Surgical Colorectal Audit reported CRM positivity rates of 7.9% and 11% for high and low-volume hospitals, respectively, and the National Bowel Cancer Audit found CRM positivity rates of 8.2% in the United Kingdom.[13,25] Patients with locally invasive T4 rectal cancer are at high risk of positive resection margins. The CRM positivity rates for T4 rectal cancer found in this study are in line with previous reports. De Nes *et al.*, for instance, showed a CRM positivity rate of 17.1%, and the PelvEx Collaborative reported a CRM positivity rate of 15.5% in an international analysis including 27 international specialized centres.[26,27]

Because of advances in imaging modalities, surgical techniques and neoadjuvant therapies, increasing numbers of patients with T4 rectal cancer will likely become eligible for curative surgery. PE is technically challenging and high-risk surgery that is ideally performed in a specialized multidisciplinary setting, involving surgical specialties such as colorectal, gynae-oncology, urology, plastic surgery, orthopaedics, and vascular surgery but currently these resources are not available in all ANZ centres treating rectal cancer.[28] Previous studies have shown that centralized care for patients requiring PE, involving experienced multidisciplinary teams, reduces CRM positivity, postoperative complications and morbidity rates.[9,12] Venchiarutti *et al.*, for instance, investigated PE outcomes from a high-volume centre in Australia that receives referrals from across the country and found that despite an increase in more extensive resections, CRM positivity rates decreased from 34% to 23.9%, and postoperative mortality also decreased.[29] These results

indicate that higher patient volumes improve both oncologic outcomes and postoperative mortality. Other centres, including ours, have reported results from a mid-volume centre with comparable CRM positivity (18.6%) and postoperative mortality rates (1.9%).[30] This suggests that, in selected patients, PE can be performed in a mid-volume centre with acceptable outcomes, provided that adequate facilities and resources are available.

Centralizing low-volume surgery can be disadvantageous for patients living in remote areas, increasing the travel burden of these often elderly and frail patients, reducing accessibility to neoadjuvant therapy, surgery and follow-up.[31] Interestingly, a study by Finlayson *et al*. found that almost half of the patients preferred treatment locally even after being informed about increased postoperative risks.[32] As well as considering patient preferences, patients living rurally should ideally be discussed at regional or state-wide multidisciplinary meetings before treatment. In case of locally invasive rectal cancer, rural patients should be considered for treatment in a high-volume centre appropriately equipped for PE.[10] Neoadjuvant and adjuvant treatment, and follow-up can still potentially be performed closer to home at the regional hospital, minimizing the travel burden.

Some limitations of this study must be addressed. Firstly, not all ANZ hospitals performing rectal cancer surgery register data in the BCCA. Historically it has been mostly larger teaching hospitals that participate, inflicting bias with underrepresentation of rural, private and low-volume hospitals.[16,17] This therefore may have underestimated the true positive margin rate on a population level. Also, number of patients registered in the BCCA varies largely between regions with SA registering four times more patients per 100 000 inhabitants than QLD and NSW. Therefore, when interpreting results, regions with higher registration compliance may have lower inclusion bias, possibly better reflecting the true results.

Furthermore, data registry of the patients that are entered to the BCCA is frequently incomplete, making it challenging to conduct certain analyses. These issues have now been addressed since in 2018 BCCA participation has become mandatory for all teaching hospitals to improve registration to better represent all regions in ANZ.

Separate registration for treatment of patients with locally invasive (T4) rectal cancer undergoing PE surgery is not included in the BCCA, leaving this vulnerable group not well documented. In particular, it remains unclear whether patients were recorded as curative or palliative based on pre-treatment intent or post-treatment outcome and pathology, so we could not correct for this in our analysis. Finally, requested de-identified hospital level data were not provided by the BCCA, and therefore we could not compare the outcomes of high-volume versus low-volume PE centres.

In conclusion, positive resection margins and rates of multivisceral resection vary between the different regions of ANZ. Patients with T4 rectal cancer are at particularly risk, which further supports the concept of referral to specialized exenteration centres for potentially curative multi-visceral resection.

Acknowledgements

The Binational Colorectal Cancer Audit (BCCA) is a collaborative project that collects data from public and private health services in Australia and New Zealand. BCCA is endorsed by CSSANZ, RACS, GSA, NZAGS and MOGA. The data in this publication are only available with the cooperation of all the participating sites, participating clinicians, and by approval of the BCCA Governance Committees. Guidelines have been applied to its use. The authors extend their thanks to all collaborators for the provision of the data. The reporting of these data are the responsibility of the authors and should not be seen as an official interpretation of the BCCA.

TLD: was supported personally by: Stichting Prof. Michaël-van Vloten Fonds. HMK: This project was undertaken whilst holding a Royal Adelaide Hospital Florey Fellowship. Open access publishing facilitated by The University of Adelaide, as part of the Wiley - The University of Adelaide agreement via the Council of Australian University Librarians.

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Tessa Dinger: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; validation; visualization; writing – original draft. **Hidde Kroon:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – review and editing. **Luke Traeger:** Data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; writing – review and editing. **Sergei Bedrikovetski:** Data curation; formal analysis; investigation; methodology; project administration; resources; software; validation; writing – review and editing. **Andrew Hunter:** Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; resources; software; supervision; writing – review and editing. **Tarik Sammour:** Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – review and editing.

Conflict of interest

None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix S1. Supporting information.