Original Research

Aortic calcification is associated with non-infective rather than infective postoperative complications following colorectal cancer resection: an observational cohort study.

Katrina A Knight MBChB, Chui Hon Fei BMedSci, Kate F Boland BMedSci, Daniel R Dolan BMedSci, Allan M Golder MBChB, Donald C McMillan PhD, Paul G Horgan PhD, Douglas H Black MBChB, James H Park PhD, Campbell SD Roxburgh PhD.

Corresponding author:

Katrina Knight

Academic Unit of Colorectal Surgery

University of Glasgow

Level 2, New Lister Building

Glasgow Royal Infirmary

10 – 16 Alexandra Parade

Glasgow G31 2ER, UK

Email: Katrina.Knight@glasgow.ac.uk

Word count: 3009

Keywords: Calcification, Physiologic; Colorectal Neoplasms; Digestive System Surgical Procedures.

Key points:

- Aortic calcification measured by visual quantification of the number of calcified quadrants at two aortic levels on preoperative CT is associated with clinical outcome following colorectal cancer surgery
- An increased burden of aortic calcification was associated with non-infective complications but not anastomotic leak
- Assessment of the degree of aortic calcification may help identify patients at risk of cardiorespiratory complications, improve preoperative risk stratification and assignment of preoperative strategies to improve fitness for surgery

Abbreviations

AC - aortic calcification

AL – anastomotic leak

ASA – American Society of Anaesthesiology

CD - Clavien-Dindo

CI – confidence interval

CRC – colorectal cancer

ICC - intraclass correlation coefficient

OR – odds ratio

ROC – Receiver Operating Characteristic

TNM – Tumour, Nodes, Metastases

Abstract

Objectives: Complications following colorectal cancer resection are common. The degree of aortic calcification (AC) on CT has been proposed as a predictor of complications, particularly anastomotic leak. This study assessed the relationship between AC and complications in patients undergoing colorectal cancer resection.

Methods: Patients from 2008-2016 were retrospectively identified from a prospectively-maintained database. Complications were classified using the Clavien-Dindo (CD) scale. Calcification was quantified on preoperative CT by visual assessment of the number of calcified quadrants in the proximal and distal aorta. Scores were grouped into categories: none, minor (<median AC score) and major (>median AC score). The relationship between clinicopathological characteristics and complications was assessed using logistic regression.

Results: Of 657 patients, 52% had proximal AC (>median score (1)) and 75% had distal AC (>median score (4)). AC was more common in older patients and smokers. Higher burden of AC was associated with non-infective complications (proximal AC 28% vs 16%, p=0.004, distal AC 26% vs 14% p=0.001) but not infective complications (proximal AC 28% vs 29%, p=0.821, distal AC 29% vs 23%, p=0.240) or anastomotic leak (proximal AC 6% vs 4%, p=0.334, distal AC 7% vs 3%, p=0.077). Independent predictors of complications included open surgery (OR 1.99, 95%CI 1.43 – 2.79, p=0.001), rectal resection (OR 1.51, 95%CI 1.07 – 2.12, p=0.018) and smoking (OR 2.56, 95%CI 1.42 – 4.64, p=0.002).

Conclusions: These data suggest that high levels of AC are associated with non-infective complications after colorectal cancer surgery and not anastomotic leak.

Introduction

Colorectal cancer remains one of the most common cancers globally, with 1.8 million new cases and over 880,000 deaths in 2018 [1]. Surgical resection is often curative in stage I to III disease. Despite improvements in surgical technique and perioperative care, postoperative complications occur in up to 50% [2–4], predisposing to delays in adjuvant therapy, higher recurrence rates and impaired survival [5–7]. Early identification of patients most at risk is therefore key in reducing postoperative complications.

Host factors predictive of postoperative complications include increasing age, the presence of comorbidity, most often represented by the American Society of Anaesthesiologists (ASA) classification, [8] and a history of smoking [9]. However, age is non-modifiable ASA is subjective and lacks inter-rater reliability while smoking cessation requires a minimum period of 8 weeks to produce a beneficial effect on surgical outcome [10].

Radiologic assessment of adverse characteristics offers a non-invasive and personalised method of preoperative risk stratification. Coronary arterial calcification quantified on CT is an established predictor of future cardiovascular events in asymptomatic populations [11–13]. Recently, the degree of aortic calcification (AC) on the preoperative CT of patients undergoing abdominal surgery was independently associated with higher rates of complications [14]. The presence of major AC was prognostic of anastomotic leak following oesophagectomy in both discovery [15] and validation [16] cohorts. However, studies in patients undergoing colorectal resection have been hampered by small sample sizes, inclusion of patients undergoing emergency surgery and differences in the underlying pathology, operative indication and technique, all of which influence complication rates [17–22].

Critically, previous studies have failed to assess the full spectrum of complications (all, major, infective and non-infective complications) and do not account for the fact that AC is influenced by shear stress and varies throughout the length of the aorta [23]. Sites of anatomical branching such as the origin of mesenteric arteries and the bifurcation are disproportionately affected [24].

AC may help to identify those at highest risk of postoperative complications, rationalise the use of limited resources such as cardiopulmonary exercise testing and prehabilitation programmes and facilitate consideration of alternative surgical strategies (e.g. end stoma formation in patients at high risk of anastomotic leak). However, its relationship with clinical outcome following colorectal cancer resection first requires clarification. This study aimed to assess the relationship between the site and burden of abdominal AC and postoperative complications following colorectal cancer resection.

Material and methods

Consecutive patients undergoing potentially curative resection of colorectal cancer at a single institution were retrospectively identified from a prospectively-maintained database. The main inclusion criterion for this observational cohort study was the availability of pre-operative staging CT images within 6 months prior to surgery. Axial images of the chest, abdomen and pelvis acquired following intravenous contrast for colorectal cancer staging purposes were used. Exclusion criteria included a history of concurrent cancer, pathology other than adenocarcinoma or known metastatic disease at the time of surgery. Patients who underwent palliative or emergency procedures and those undergoing endoscopic management of polyp cancers or transanal resection of rectal cancers were also excluded.

Clinical and pathological data including perioperative complications were recorded prospectively. Pathological tumour stage was reported using the TNM staging system [25]. Complications within 30 days were graded using the Clavien-Dindo scale (I to V) according to the treatment required; complications requiring surgical intervention are regarded as major and classified as grade III and above [26]. Additionally, complications were classified as infective and non-infective [27]. Non-infective complications included persistent ileus, pulmonary embolus and cardiac events encompassing acute coronary syndrome and acute myocardial infarction. Infective complications included surgical site infections (wound or intra-abdominal (abscess/anastomotic leak)) and remote site infections (e.g. pneumonia). Anastomotic leak was defined as a communication between the intra- and extraluminal compartments arising from a defect in the intestinal wall at the anastomotic site [17]. Cases of suspected leak were confirmed on CT and verified by a radiologist.

To assess the degree of AC, a novel semi-quantitative visual assessment method was used. Calcification in the proximal and distal aorta was evaluated on three transverse images. The proximal aorta at the level of the superior mesenteric artery was located, its circumference divided into quadrants and a point assigned for each calcified quadrant. A slice showing the distal aortic circumference in its entirety immediately proximal to the bifurcation was then selected and the same scoring methodology applied. A slice immediately distal to the bifurcation was used to score the circumference of both common iliac arteries. Examples are displayed in Figures 1-3.

For proximal AC, a maximum score of 4 was possible. For distal AC, a score of 0 to 4 was possible for each of the three vessels: the distal aorta immediately proximal to the bifurcation and each common iliac artery at their origin. These were summed to provide a combined distal AC score with a maximum of 12.

Several approaches were used to identify the optimal method of grouping patients into clinically relevant categories according to the degree of calcification present at each site. ROC analysis of the relationship between calcification score and any complication as the state variable was undertaken (supplementary data). This failed to identify a statistically significant threshold that enabled patients with minor and major calcification to be distinguished. Similar to previously published work, the degree of calcification was grouped in to categories using the median: absent (score 0), minor (less than median) or major (greater than median) [14]. Tertile values for continuous proximal and distal AC scores were also derived and found to closely align with the median values (supplementary data). The median value was therefore used to derive calcification categories.

The scoring system was devised by a radiologist (DHB) and surgeon (JHP) at the same institution who instructed a surgical trainee (KK) in its application using a training sample of 150 scans. All scans from the study cohort were assessed separately by two individuals (KK, CHF). A further sample of 30 scans was analysed by a group of five surgeons (KK, CHF, KB, DD, AG) to assess inter-rater reliability and re-assessed by one individual (KK) after a 4 week interval to assess intra-rater reliability. All assessors were blinded to clinicopathological characteristics at the time of scan assessment.

This study was approved by the regional research ethics committee (reference number 17/WS/0200). The need for informed consent from patients was waived due to the retrospective nature of the study.

Statistical analysis

Descriptive statistics were used to summarise baseline characteristics. The Mantel-Haenszel test was used to assess associations between the degree of AC and clinicopathological characteristics. Binary logistic regression analysis was used to determine relationships between clinicopathological characteristics and postoperative complications. Variables with a p-value of less than 0.05 on univariate analysis were included in the multivariate model using a backward conditional method. The intraclass correlation coefficient (ICC) was used to compare inter- and intra-rater reliability. ICC estimates and their 95% confident intervals were calculated based on a mean-rating, absolute-agreement, 2-way mixed-effects model. An ICC less than 0.5 was considered poor, between 0.5 and 0.75 moderate, 0.75 to 0.9 good and greater than 0.9 excellent [28]. A p value < 0.05 was considered significant. Statistical analysis was performed using SPSS software (version 25.0; SPSS Inc.).

Results

Between 2008 and 2016, 820 patients underwent colorectal resection. Following exclusion of patients who had surgery for recurrent disease, local resection, emergency or palliative procedures and distant metastatic disease at time of surgery, 672 patients were included. Pre-operative CT imaging was not available in 7 patients and unsuitable for analysis for technical reasons including significant aortic contrast (6 patients) and aberrant vascular anatomy (2 patients). The baseline demographic and clinicopathological characteristics of the remaining 657 patients are presented in Table 1.

Most patients were male (56%), aged over 65 years (63%) and ASA grade one or two (68%). The median age was 68 years (range 27-93). Current or ex-smokers comprised 55% of the study cohort. The majority of patients had pathological T-stage 3 (55%) and node-negative (65%) disease. Open surgery was undertaken in 405 patients (62%).

For intra-rater reliability, the ICC was 1.0 for proximal AC and 0.97 (95% CI 0.96 – 0.98) for distal AC. For inter-rater reliability, the ICC for proximal AC was 0.89 (95% CI 0.82 – 0.94) and for distal AC was 0.92 (95% CI 0.87 – 0.96).

When assessing proximal AC, 315 (48%) patients had no calcification and 342 (52%) had visible calcification; the median proximal AC score in those with calcification was 1 (range 1 to 4). For distal AC, 163 (25%) patients had no calcification and 494 patients (75%) had visible calcification; the median score was 4 (range 1 to 12). Proximal AC was categorised as minor in 208 patients (32%) and major in 134 patients (20%). Distal AC was minor in 234 patients (35%) and major in 260 patients (40%). Both proximal and distal AC were present in 322 patients (49%), proximal AC alone present in 20 patients

(3%) and distal AC alone in 172 patients (26%). Examples of the spectrum of proximal and distal AC are depicted in Figures 1-3.

Postoperative complications of any grade developed in 282 patients (43%), of which 60 (9%) were major complications (Clavien-Dindo grade III or higher). Infective complications developed in 185 patients (28%) while non-infective complications occurred in 131 (20%) patients (Table 2).

The associations between the degree of aortic calcification and clinicopathological characteristics are shown in Table 3. For proximal AC, increasing age ($p<0.001$), higher ASA grade ($p<0.001$), positive smoking history ($p<0.001$), colonic tumour site ($p=0.025$) and higher T stage ($p=0.018$) were associated with increasing burden of calcification. For distal calcification, similar associations with increasing age ($p<0.001$), ASA grade ($p<0.001$) and positive smoking history ($p<0.001$) as well as male gender ($p=0.002$) were associated with increasing burden of calcification.

The associations between AC and postoperative complications are displayed in Table 4. Proximal AC was associated with the development of non-infective complications (28% vs 16%, $p=0.004$) but not major or infective complications. Distal AC was associated with the development of all complications (47% vs 34%, $p=0.015$), major complications (12% vs 5%, $p=0.015$) and non-infective complications (26% vs 14%, $p<0.001$).

Anastomotic leak occurred in 30 of 562 patients who underwent anastomosis formation (5.3%), with 22 patients (73%) requiring relaparotomy. The rate of AL was similar at 4.6% when patients who had defunctioning ileostomies (n=110) during the index procedure were excluded. The majority of patients (n=24, 80%) who developed AL had undergone anterior resection. There was no association between the presence of proximal AC and AL. A non-significant trend was noted between distal AC and AL (7% vs 3%, p=0.077).

Logistic regression was performed to determine the relationship between clinicopathological characteristics and all postoperative complications (Table 5). On univariate analysis, increasing age (OR 1.24, 95%CI 1.01 – 1.51, p=0.040), male gender (OR 1.54, 95% CI 1.13 – 2.11, p=0.007), higher ASA grade (OR 1.53, 95% CI 1.10 – 2.12, p= 0.012), positive smoking history (OR 1.76, 95% CI 1.29 – 2.42, p = 0.001), rectal tumour site (OR 1.49, 95%CI 1.08 – 2.07, p=0.014), open surgery (OR 2.54 (95%CI 1.54 – 2.97), p=0.001) and the presence of distal AC (OR 1.28, 95% CI 1.05 – 1.56, p=0.015) were associated with the development of postoperative complications. On multivariate analysis, factors which were independently predictive of postoperative complications included male gender (1.50, 95%CI 1.08 - 2.07, p=0.015), rectal tumour site (OR 1.51, 95%CI 1.07 – 2.12, p=0.018) and open surgery (OR 1.99, 95%CI 1.43 – 2.79, p=0.001).

Logistic regression was also performed to determine the relationship between clinicopathological characteristics and major complications (CDIII-V) (Table 5). On univariate analysis, positive smoking history (OR 2.56, 95%CI 1.42 – 4.64, p=0.002) and the presence of distal AC (OR 1.56, 95%CI 1.08 – 2.24, p=0.016) were related to major complications. However, on multivariate analysis, a positive smoking history was the only independent predictive of major complications (OR 2.56, 95%CI 1.42 – 4.64, p=0.002).

Finally, logistic regression was performed to determine the relationship between clinicopathological characteristics and non-infective complications (Table 5). On univariate analysis, increasing age (OR 1.64, 95%CI 1.27 – 2.12, p=0.001), open surgery (OR 1.54, 95%CI 1.02 – 2.32, p=0.041), an increased burden of proximal AC (OR 1.42, 95%CI 1.12 – 1.81, p=0.004) and distal AC (OR 1.53, 95%CI 1.19 – 1.98, p=0.001) were associated with the development of non-infective complications. On multivariate analysis, age was the sole independent predictor of non-infective complications (OR 1.48, 95%CI 1.12 – 1.96, p<0.001).

Discussion

This study demonstrates that it is possible to visually assess AC on routinely-obtained CT imaging and that an increased burden of AC is related to non-infective rather than infective complications. Calcification was quantified with relative ease and excellent reproducibility. Associations between increasing levels of AC and cardiovascular risk factors including increasing age, ASA grade and smoking suggest that this novel and simple method captured clinically-relevant atherosclerotic disease without the need for dedicated imaging software. The consistent association between an increasing degree of AC and non-infective complications suggests that AC may have a role to play in identifying patients at risk of non-infective complications and cardiac-related peri-operative events.

The recent expansion of perioperative medicine has facilitated detailed assessment of high-risk patients in dedicated clinics [29]. Such review has been shown to reduce risk of complications through preoperative optimisation using multimodal prehabilitation, improved critical care use and enhanced shared decision-making between surgeons, anaesthetists and patients [30]. However, defining the high-risk patient and balancing demand with resource capacity remain challenging. To this end, characterisation of the frailty phenotype with static and dynamic markers that are readily available and are applicable by staff from differing specialties is highly desirable. At individual patient level, a high burden of AC may form part of the criteria used to trigger consideration of high-risk clinic review and further investigation of cardiac functional status. At organisational level, the presence of significant AC in combination with existing indicators of adverse outcome e.g. advanced age may aid decision-making regarding appropriate post-operative destination (i.e. critical care or ward level). As the population aged over 60 continues to expand [31] and the incidence of colorectal cancer continues to rise [32], radiographic biomarkers such as AC may assist with pragmatic resource utilisation in an increasingly burdened healthcare system.

Characterising the high-risk patient calls for subsequent intervention to mitigate risk. Improvements in cardiorespiratory fitness gained through preoperative exercise programmes correlate with reduced postoperative complications following CRC resection [33–35]. However, prehabilitation trial participants are often younger and less comorbid than non-trial participants [36]. Future trials and service development may be better served by including a radiographic biomarker e.g. AC in combination with myopenia as an inclusion criterion. Such markers are attractive as they represent personalised and cost-effective methods of identifying higher risk patients who are not detected by current subjective measures such as ASA grading.

A history of smoking was the only independent predictor of major complications in this study. Smoking accelerates atherosclerosis through vascular inflammation and endothelial dysfunction and is independently related to subclinical atherosclerosis [37]. However, smoking is strongly correlated with infective rather than non-infective complications [9]. Distal AC was also associated with increased odds of major complications but was not independent of smoking or open surgery. While smoking cessation has been associated with reduced complication rates, it requires intensive interventions over a period of several weeks, limiting its utility in patients managed within time-targeted cancer pathways [10]. Non-modifiable factors such as male gender and rectal cancer were associated with higher odds of complications while open surgery was an independent predictor of all complications. Use of minimally invasive approaches including robotic surgery for rectal cancer with its ergonomic advantages in restricted areas such as the male pelvis represents a feasible strategy to reduce postoperative complications and the attendant consequences [38].

The disparity between our results and previous studies investigating AC and anastomotic leak warrants discussion. Thoracic AC was independently associated with leak following oesophagectomy [15, 16]. Unlike the mesenteric arteries, thoracic aortic branches are end arteries and AC here is more likely to impact on anastomotic healing. In colorectal surgery, the accepted leak rate is below 10% [39]. Leak rates in colorectal studies examining AC have ranged from 8 to 22% [17–20, 22]. The leak rate was low at 5% among the 562 patients who underwent a primary anastomosis in this cohort. Moreover, all patients in this study underwent elective resection according to the principles of oncologic surgery. By comparison, four of six studies examining AC and leak included benign disease (e.g. diverticular disease) and emergency operations, both of which can influence complication rates [18–21]. One study of patients undergoing CRC resection in Iran reported a leak rate of 20% but included only patients with ASA grades 1 or 2 in whom CVD risk is likely to be low [17]. Shen and colleagues reported a leak rate of 7.8% among 423 Chinese patients undergoing rectal cancer resection and found an independent relationship between AC and leak [22]. In addition to the lower incidence of radiographically-detectable vascular calcification in Asian populations [8], the authors highlighted the low predictive value of the AC threshold derived in this cohort, suggesting the reported relationship with leak is not directly comparable to patients from Europe and North America.

This study has several limitations. Its single-centre nature limits generalisability to the wider population undergoing colorectal resection. The use of visual AC quantification is subject to bias, although investigators were blinded to clinicopathological data at the time of scan assessment. Mesenteric vascular abnormalities including stenosis or occlusion were not assessed due to previous work suggesting asymptomatic stenosis (<50% or >50%) or occlusion is not associated with adverse outcome [40]. Comparison of visual and software AC assessment represents an important methodological aspect requiring evaluation. However, commercial calcium-scoring software is designed for cardiac imaging. Its use on non-gated, contrast-enhanced imaging is not recommended due to the risk of overestimation [41]. To define a potential role in preoperative risk assessment, investigating the relationship between AC and dynamic functional assessments such as cardiopulmonary exercise testing is a key target for future work.

In conclusion, radiographically-detectable aortic calcification is associated with post-operative complications following colorectal cancer resection and may aid in identification of patients who could benefit from additional pre-operative investigation and optimisation. Further work to validate these findings is required.

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Table 1: Baseline characteristics of patients undergoing elective resection of non-metastatic colorectal cancer between 2008 - 2016 (n = 657).

Characteristic		n (%)
Age (years)	< 65	241 (37)
	65 – 75	259 (39)
	> 75	157 (24)
Gender	Male	368 (56)
	Female	289 (44)
ASA grade	1	144 (22)
	2	303 (46)
	3	188 (29)
	4	22 (3)
BMI	< 30	428 (65)
	> 30	218 (33)
	Not recorded	11 (2)
Smoking status	Non-smoker	297 (45)
	Ex-smoker	266 (41)
	Current	94 (14)
Tumour site	Colon	426 (65)
	Rectum	231 (35)
Surgical approach	Open	405 (62)
	Laparoscopic	252 (38)
T stage	0[a]	10 (1)
	1	89 (13)
	2	98 (15)
	3	358 (55)
	4	102 (16)
N stage	0	430 (65)
	1	167 (25)

	2	60 (9)

Abbreviations: ASA – American Society of Anaesthesiologists, BMI – body mass index.

a T Stage 0 – 10 patients with rectal cancer had complete pathologic response following neoadjuvant chemoradiation.

Table 2: Frequency of complications.

Complication type	Frequency n (%)
Any	280 (43)
Major (Clavien-Dindo grade III or greater)	60 (9)
Infective (total)	185 (28)
Surgical site infection	122 (19)
Remote site infection	63 (9)
Non-infective	131 (20)

Table 3: Association between the degree of proximal and distal aortic calcification and clinico-pathological characteristics of patients undergoing colorectal cancer resection (Mantel-Haenszel test, significance level p<0.05).

		Proximal AC				Distal AC			
		None n=315 (48%)	Minor n=208 (32%)	Major n=134 (20%)	p-value	None n=163 (25%)	Minor n=234 (35%)	Major n=260 (40%)	p-value
Age	< 65	189 (78)	39 (16)	13 (6)	0.001	112 (47)	90 (37)	39 (16)	0.001
	65 – 75	96 (37)	103 (40)	60 (23)		42 (16)	98 (38)	119 (46)	
	> 75	30 (19)	66 (42)	61 (39)		9 (6)	46 (29)	102 (65)	
Gender	Male	168 (46)	132 (36)	68 (18)	0.889	79 (21)	125 (34)	164 (45)	0.002
	Female	147 (51)	76 (26)	66 (23)		84 (29)	109 (38)	96 (33)	
ASA grade	1 – 2	245 (55)	136 (30)	66 (15)	0.001	133 (30)	174 (39)	140 (31)	0.001
	3 - 4	70 (33)	72 (34)	68 (32)		30 (14)	60 (29)	120 (57)	
BMI[a]	< 30	200 (47)	131 (30)	97 (23)	0.112	112 (26)	124 (29)	192 (45)	0.073
	> 30	111 (51)	71 (33)	36 (16)		49 (23)	105 (48)	64 (29)	
	Non-smoker	167 (56)	82 (28)	48 (16)	0.001	122 (41)	105 (35)	70 (23)	0.001

Smoking status	Ex-smoker	112 (36)	92 (35)	62 (23)		28 (10)	103 (39)	135 (51)	
	Current	36 (38)	34 (36)	24 (26)		13 (14)	26 (28)	55 (58)	
Tumour site	Colon	190 (45)	142 (33)	94 (22)	0.025	100 (24)	149 (35)	177 (41)	0.144
	Rectum	125 (54)	66 (29)	40 (17)		63 (27)	85 (37)	83 (36)	
		Proximal AC				Distal AC			
		None n=315 (48%)	Minor n=208 (32%)	Major n=134 (20%)	p-value	None n=163 (25%)	Minor n=234 (35%)	Major n=260 (40%)	p-value
T stage[b]	1 – 2	109 (55)	55 (28)	33 (17)	0.018	52 (26)	73 (37)	72 (37)	0.327
	3 – 4	206 (45)	153 (33)	101 (22)		111 (24)	161 (35)	188 (41)	
N-stage	N0	198 (46)	139 (32)	93 (22)	0.157	108 (25)	144 (34)	178 (41)	0.498
	N≥1	117 (52)	69 (30)	41 (18)		55 (24)	90 (40)	82 (36)	

Abbreviations: AC – aortic calcification, ASA – American Society of Anaesthesiologists, BMI – body mass index.

[a] Missing cases: BMI - 11.

[b] T stage 0 incorporated into T stage groups 1 – 2

Table 4: Associations between the degree of proximal and distal aortic calcification and postoperative complications in patients undergoing colorectal cancer resection (Mantel-Haenszel test, significance level p<0.05).

		Proximal AC				Distal AC			
		None **n = 315 (48%)**	**Minor** **n = 208 (31%)**	**Major** **n = 134 (20%)**	**p-value**	**None** **n = 163 (25%)**	**Minor** **n = 234 (35%)**	**Major** **n = 260 (40%)**	**p-value**
All complications	**No**	188 (60)	117 (56)	70 (52)	0.138	107 (66)	130 (56)	138 (53)	0.015
	Yes	127 (40)	91 (44)	64 (48)		56 (34)	104 (44)	122 (47)	
Major complications	**No**	286 (91)	192 (92)	119 (89)	0.661	155 (95)	213 (91)	229 (88)	0.015
	Yes	29 (9)	16 (8)	15 (11)		8 (5)	21 (9)	31 (12)	
Infective complications	**No**	225 (71)	150 (72)	97 (72)	0.821	126 (77)	161 (69)	185 (71)	0.240
	Yes	90 (29)	58 (28)	37 (28)		37 (23)	73 (31)	75 (29)	
Anastomotic leak[a]	**No**	264 (96)	167 (94)	101 (94)	0.334	143 (97)	191 (96)	198 (93)	0.077
	Yes	12 (4)	11 (6)	7 (6)		5 (3)	9 (4)	16 (7)	
Non-infective complications	**No**	264 (84)	166 (80)	96 (72)	0.004	140 (86)	195 (83)	191 (74)	0.001
	Yes	51 (16)	42 (20)	38 (28)		23 (14)	39 (17)	69 (26)	

Abbreviations: AC – aortic calcification.

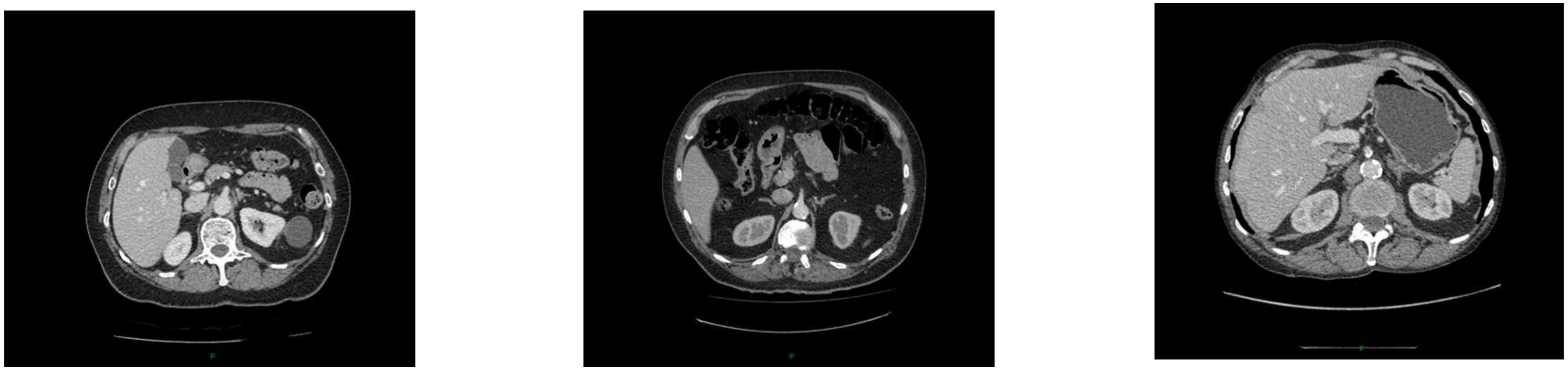
Table 5: Analysis of the relationship between clinico-pathological characteristics and postoperative complications in patients undergoing colorectal cancer resection (Binary logistic regression, significance level p<0.05).

	All complications				Major complications				Non-infective complications			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (<65 / 65-74/>75)	1.24 (1.01 – 1.51)	0.040	1.23 (0.993 – 1.53)	0.057	1.35 (0.96 – 1.90)	0.090	-	-	1.64 (1.27 – 2.12)	0.001	1.48 (1.12 – 1.96)	0.001
Sex (Female/Male)	1.54 (1.13 – 2.11)	0.007	1.50 (1.08 – 2.07)	0.015	1.03 (0.60 – 1.76)	0.915	-	-	1.25 (0.84 – 1.84)	0.269	-	-
ASA grade (I-II/III-IV)	1.53 (1.10 – 2.12)	0.012	1.37 (0.97 – 1.94)	0.077	1.47 (0.85 – 2.54)	0.163	-	-	1.30 (0.87 – 1.94)	0.200	-	-

Smoking history (No/Yes)	1.76 (1.29 – 2.42)	0.001	1.40 (0.89 – 2.19)	0.147	2.56 (1.42 – 4.64)	0.002	2.56 (1.42 – 4.64)	0.002	1.34 (0.91 – 1.98)	0.137	-	-
BMI (<30/ >30 kg/m^2)	1.36 (0.98 – 1.89)	0.068	-	-	0.71 (0.39 – 1.29)	0.261	-	-	0.83 (0.55 – 1.26)	0.382	-	-
	All complications				Major complications				Non-infective complications			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Tumour site (Colon/rectum)	1.49 (1.08 – 2.07)	0.014	1.51 (1.07 – 2.12)	0.018	1.16 (0.67 – 2.01)	0.589	-	-	1.08 (0.73 – 1.61)	0.692	-	-

Surgical approach (Laparoscopic/ Open)	2.54 (1.54 – 2.97)	0.001	1.99 (1.43 – 2.79)	0.001	1.17 (0.67 – 2.04)	0.575	-	-	1.54 (1.02 – 2.32)	0.041	1.47 (0.97 – 2.23)	0.071
TNM stage (I – II/III)	1.15 (0.83 – 1.59)	0.395	-	-	1.01 (0.58 – 1.77)	0.960	-	-	1.07 (0.82 – 1.59)	0.752	-	-
Proximal AC (None / Minor/ Major)	1.16 (0.95 – 1.42)	0.138	-	-	1.08 (0.77 – 1.51)	0.660	-	-	1.42 (1.12 – 1.81)	0.004	1.08 (0.80 – 1.46)	0.624
Distal AC (None / Minor / Major)	1.28 (1.05 – 1.56)	0.015	1.05 (0.83 – 1.33)	0.703	1.56 (1.08 – 2.24)	0.016	1.32 (0.90 – 1.94)	0.158	1.53 (1.19 – 1.98)	0.001	1.27 (0.96 – 1.69)	0.099

Figure 1: Examples of proximal aortic calcification.

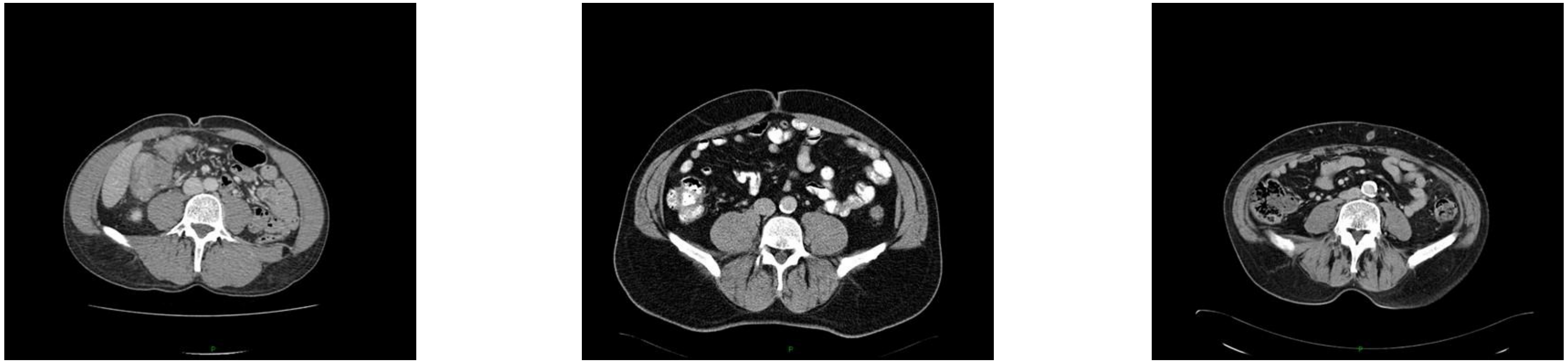


(a) No calcification (score 0)

(b) Minor calcification (score 2)

(c) Major calcification (score 4)

Figure 2: Examples of distal aortic calcification.



(a) No calcification (score 0)

(b) Minor calcification (score 2)

(c) Major calcification (score 4)

Figure 3: Examples of common iliac arterial calcification.

(a) No calcification (score 0 for each common iliac)

(b) Minor calcification (score 2 for each common iliac)

(c) Major calcification (score 4 for each common iliac)