Title: The Relationship Between Body Mass Index, Sex, and Postoperative Outcomes in Patients Undergoing Potentially Curative Surgery for Colorectal Cancer

Arwa S Almasaudi [1,2], Stephen T McSorley [1], Paul G Horgan, Donald C McMillan [1], Christine A Edwards [2]

1. Academic Unit of Surgery, College of Medical, Veterinary and Life of Sciences- University of Glasgow, Royal Infirmary, Glasgow G31 2ER.

2. Human Nutrition, School of Medicine, Dentistry and Nursing, College of Medical, Veterinary and Life of Sciences University of Glasgow, Glasgow Royal Infirmary, Glasgow, G31 2ER.

Correspondence to;

Arwa Almasaudi,

Human Nutrition, School of Medicine, University of Glasgow, New Lister Building

Glasgow Royal Infirmary, Alexandra Parade. Glasgow G31 2ER

Email: a.almasaudi.1@research.gla.ac.uk

Running Head: BMI and postoperative outcomes in patients with colorectal cancer.

List of abbreviations:

SIR: Systemic Inflammatory Response.

mGPS: modified Glasgow Prognostic Score

Post-op GPS: Post-Operative Glasgow Prognostic Score

NLR: Neutrophil-to-lymphocyte Ratio

SSI: Surgical Site Infection

Abstract

Background

There is increasing evidence that an increased BMI is associated with increased complications after surgery for colorectal cancer (CRC). However, the basis of this relationship is not clear. Since men and women have different fat distribution, with men more likely to have excess visceral fat in BMI defined obesity, there may be a sex difference in the surgical site infection (SSIs) rate in the obese. Therefore, the aim of this study was to examine the relationship between sex, BMI, clinic-pathological characteristics and the development of postoperative infective complications after surgery for CRC and to establish whether there were gender differences in complication following surgery for CRC.

Design

Data were recorded prospectively for patients undergoing potentially curative surgery for CRC in a single centre between 1997 and 2016. Patient characteristics were recorded and complications were classified as either infective or non-infective. The relationship between sex, BMI, associated clinicopathological characteristics and presences of complications were examined by Chi-square test for linear association and multivariate binary logistic regression model.

Results

A total of 1039 patients were included. There were significant differences in the presence of complications between male and female ($p \leq 0.001$), the rate of complication was higher in obese male (44%); in particular SSIs, wound infection and anastomotic leak ($p \leq 0.05$). The rate of surgical site infection was 12% in male patients with normal BMI compared with 26% in those with a BMI ≥ 30 ($p \leq 0.001$), while the rate of SSIs in female patients was 10% in

those with normal BMI and those with a BMI ≥30. In males, BMI remained significantly associated with SSI on multivariate analysis [(OR =1.42, 95% CI 1.13-1.78) P=0,002].

Conclusions

Obesity prior to surgery for CRC increases the risk of infective complications in both male and female. Increased BMI in male patients was associated greater risk of SSIs and wound infection compared to female patients. Male obese patients should be considered at high risk of developing post-operative infective complications.

1-Introduction:

The prevalence of obesity is increasing globally and has become a major public health concern. In the United Kingdom, the prevalence of obesity has increased dramatically over the past few years to such an extent that approximately 30% of the population had a body mass index (BMI) over 30. The UK now has the highest rate of obesity in Western Europe, according to the Organisation for Economic Co-operation and Development (OECD) (1)

Obesity has been associated with increased risk of several chronic diseases, such as high blood pressure, chronic heart disease, renal disease, type 2- diabetes and many forms of cancer including colorectal cancer (2). Indeed, a meta-analysis with 70,000 cases reported that for each 2 kg/m^2 increase in BMI there was a 7% higher risk of colorectal cancer (3). This association was stronger in males than females, and sex may play a major role in disease progress and outcomes. In addition to increased risk, a large prospective study, with 900,000 subjects, reported an association between BMI and risk of death from colorectal cancer (4) Moreover, studies comparing the outcome for the two sexes have reported improved long term survival of women with colorectal cancer which is not explained by any substantial differences in extent of disease or treatment delivered (5,6). However, whether women and men show differences in short term outcomes is not well described.

Despite major advances in surgical procedures, surgical morbidity after colorectal cancer resection remains a significant problem, with infectious complications, particularly surgical site infections (SSIs), the most frequent, accounting for 30-40% of all complications (8). The National Nosocomial Infection System (NNIS) of the US Center for Disease Control and Prevention (CDC) has classified surgical site infection into superficial wound infection and deep organ/space infection, including anastomotic leak and abscess (9). It has been reported

that these complications contribute to a high rate of re-operation, increased length of hospital stay, higher hospital costs (10) and early mortality (11).

There is increasing evidence that obesity at the time of surgery is associated with increased risk of postoperative infective complications in patients with colorectal cancer. For example, it has been recently reported that patients with high BMI are at increased risk for surgical site infection following surgery for colorectal cancer, independent of other potentially confounding factors (7). An implication of this systematic review was that since, men and women have different fat distribution with men more likely to have excess visceral fat in BMI defined obesity, there may be a sex difference in the surgical site infection rate in the obese. However, to our knowledge this relationship has not been examined.

An understanding of the association between sex, obesity, and the post-operative systemic inflammatory response and complications of colorectal cancer surgery is important to evaluate the risks associated with colorectal cancer surgery. The aim of the present study, therefore, was to examine the relationship between sex, BMI, pre-and post-operative systemic inflammatory response and development of postoperative infective complications following surgery for colorectal cancer.

2-Methods

Anonymised data was prospectively collected for patients who underwent elective, potentially curative surgery for colorectal cancer in a single centre between January 1997 and February 2016. Those who underwent an emergency procedure were excluded. Recorded information included demographics, tumour site, TNM stage, surgical approach, whether neoadjuvant or adjuvant treatment was given, and the presence and type of complications.

BMI was calculated from height and weight measured at the preoperative assessment visit prior to surgery and BMI categorised according to the WHO cut-offs (normal weight 18.5-24.9, overweight 25- 29.9, obese 30-34.9, morbidly obese ≥35). A small number of patients who were classified as underweight (4% of all patients) were excluded from the analysis.

The preoperative systemic inflammatory response was assessed using the preoperative modified Glasgow Prognostic Score (mGPS), calculated from preoperative serum C-reactive protein (CRP) and albumin. Patients with a CRP ≤10mg/L were allocated a score of 0, a CRP > 10mg/L a score of 1, and a CRP >10mg/L and albumin <35g/L a score of 2. The postoperative systemic inflammatory response was assessed using the postoperative Glasgow Prognostic Score (post-op GPS). Patients with postoperative CRP concentration ≤150 mg/L were allocated a score of 0, a CRP concentration > 150 mg/L a score of 1, and CRP ≥150 mg/L and albumin <25 g/L a score of 2.

Patients were assessed for both infective and non-infective complications. Infective complications included; respiratory tract infection, urinary tract infection, or any surgical site infection. Non-infective complications included; ileus, acute coronary syndrome, acute myocardial infarction, pulmonary embolism and arrhythmias.

Surgical site infection was defined as the presence of superficial wound infection or a deep organ/space infection (including intra-abdominal abscess and anastomotic leakage). A wound infection included the presence of pus that discharged spontaneously or required drainage; an intra-abdominal abscess was confirmed by imaging and required either conservative therapy with antibiotics or drainage; an anastomotic leak was defined as a fistula to the bowel anastomosis that was confirmed radiologically or diagnosed at relaparotomy. Any uncertainties were addressed by review of electronic and/or physical case notes. The study was approved by the West of Scotland Research Ethics Committee, Glasgow.

Statistical Analysis

Categorical data regarding patient and disease characteristics were examined and compared by Chi-square test and Chi square test for linear association where appropriate. P values <0.05 were considered statistically significant. Surgical site infection was analysed using univariate and multivariate binary logistic regression model. Those variables associated to a degree of $p<0.1$ were entered into a backward conditional multivariate model. Those variables found to be significantly associated with surgical site infection were entered into a multivariate model. Statistical analyses were performed using IBM SPSS version 22 for Windows (Chicago, IL, USA).

3-Results:

A total of 1039 patients were included having undergone potentially curative surgery for colorectal cancer (587 were male and 452 were female).

3.1 Gender, clinicopathological characteristics and post-operative complications.

When the patient's demographic, pathological, and clinical characteristics were compared between male and female (Table 2), there was a significant difference in tumour site ($p \leq 0.05$), post -operative GPS day 3 ($p \leq 0.05$) and operative time ($p \leq 0.05$). There were also significant differences in the presence of complications between male and female ($p \leq 0.001$) with male having higher rate of complication (44%), in particular infective complications ($p \leq 0.05$).

3.2 The distribution of the clinicopathological characteristics and post-operative complications in male and female based on BMI.

In Table 2, male patients were classified by BMI, 33% were normal weight, 39% overweight, 19% were obese and 9% were morbidly obese. When the distribution of the clinicopathological characteristics in male patients were compared according to BMI, there was a significant association between BMI and age ($p \leq 0.05$) smoking ($p \leq 0.001$), year of surgery ($p \leq 0.05$), pre-operative mGPS ($p \leq 0.05$), NLR ($p \leq 0.001$) and neoadjuvant therapy ($p \leq 0.05$).

Among the male patients, 241(44%) experienced complications. Of these patients 160 (29%) had infective complications, where 104 (19%) had non-infective complications. When complications were compared across BMI categories, there was a significant association of BMI with the occurrence of surgical site infection ($p<0.001$) and wound infection ($p<0.001$).

The rate of surgical site infection was 12% in male patients with normal BMI compared with 26% in those with a BMI ≥30 ($p \leq 0.001$). wound infection was 7% with normal BMI compared with 20 % in those with a BMI ≥30 ($p \leq 0.001$).

In Table 4, female patients were classified by BMI, 41% were normal weight, 29% overweight, 17% were obese and 13% were morbidly obese. When the distribution of the clinicopathological characteristics in female patients were compared according to BMI, there was a significant association between BMI and age ($p \leq 0.001$), NLR ($p \leq 0.001$), ASA grade ($p \leq 0.05$), Laprascopic ($p \leq 0.05$), Post-operative GPS day 4 ($p \leq 0.001$).

Infective complication in female patients, was significantly associated with higher BMI ($p < 0.05$); in particular wound infections ($p < 0.001$). Wound infection was 6 % in female patients with normal BMI compared with 8% in those with a BMI ≥30 ($p = 0.003$). The rate of surgical site infection in female patients was 10% with normal BMI and same in those with a BMI ≥30 ($p = 0.054$). There was no significant association between BMI and non-infective complications in both male and female.

3.3 Surgical site infection, BMI and confounding factors

Among the male patients (Table 3), univariate analysis of surgical site infection, there was a significant association with BMI and age. BMI remained significantly associated with surgical site infection on multivariate analysis [(OR =1.42, 95% CI 1.13-1.78) P=0,002]. In female patients (Table 5), univariate analysis of surgical site infection detected a significant association with BMI (P=0.055), NLR>5(P=0.004), Laprascopic(0.006), post-operative day 4 GPS ($P \leq 0.001$).). On multivariate analysis of these significant variables, the inflammatory markers; NLR>5 [(OR=2.92, 95% CI 1.09-7.81) P=0.033] and post-operative day 4 GPS

188 (OR=2.22, 95% CI 1.47-3.34) P≤0.001] remained independently associated with surgical site
189 infection.

190

Discussion:

In the present study, there was a gender difference in the occurrence of complications following surgery for colorectal cancer. To our knowledge few studies address obesity and gender differences in complication. In this study, postoperative infective complications including surgical site infection and wound infection were higher in obese men, while the rate of surgical site infections in female patients was same in those with normal BMI and those with a BMI ≥30. In addition, BMI in male patients was significantly associated with surgical site infection independent of other confounding factors. Therefore, in male patients undergoing surgery for colorectal cancer obesity should be considered at high risk of developing post-operative infective complications.

The basis of the relationship between obesity and postoperative infection is not clear. This association could be in part accounted for by the magnitude of the post-operative systemic inflammatory response. It is of interest that obesity as well as cancer has a clear, but not yet precisely defined, effect on the immune function through a variety of immune mediators, including abnormal production of cytokines and acute-phase proteins (12). The excess adiposity and secretion of free fatty acids from the adipose tissue in obese patients, leads to dysregulation of adipose tissue-derived secretory factors, such as adipokines. These can trigger chronic low-grade inflammation and interact with a range of processes in metabolic tissues, including skeletal muscle and liver (12). Furthermore, the inflammatory state may play a role in the pathogenesis of many obesity related conditions, part of the metabolic syndrome, such as hyperglycaemia, insulin resistance and diabetes, and may therefore influence colorectal surgical outcomes.

Since abdominal obesity is predominant in males, the present result would indicate that the association was probably not due to differences in sex hormones but merely due to the fact that men had more fat inside the abdominal wall, which may result in more difficult resections, the need for longer incisions (13) and the need for long operative time. In addition, adiposity may affect the tissue concentrations of preoperative antibiotics (14). Furthermore, abdominal obesity is associated with metabolic abnormalities such as hyperinsulinemia and insulin resistance, as well as the release of insulin like growth factors, that are known to contribute to the proliferation and progression of malignant colonic cells and associated with poor operative outcome (15). Finally, the presence of excess visceral fat tissue in obese patients, with decreased oxygen tension and circulation, leads to increased susceptibility to infections and impaired wound healing (16). However, prior to surgery for colorectal cancer, the potential for reducing the level of obesity in the male patient is limited. Therefore, surgical management of these patients should take into account the increased risk for developing surgical site infection.

An important strength of this study is its relative large size in a detailed cohort of patients with colorectal cancer. Limitations include that the data have been retrospectively analysed. In addition, a measurement of obesity by BMI does not give insight in to the body composition changes that may be important in the development of surgical site infection. More detailed analysis of body composition including visceral fat and skeletal muscle mass assessment may provide more specific markers for post-operative complications.

In summary, the results of the present study indicate that male patients with BMI defined morbid obesity are of increased risk of surgical site infection and wound infection after surgery for colorectal cancer. This should be taken into into consideration when developing post-operative management plans. Further investigation of the association between sex, BMI,

239 body composition and the development of post-operative infective complications is

240 warranted.

241

242 Acknowledgment

243 This work was supported by the Faculty of Applied Medical Science, Clinical Nutrition

244 Department at King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia

245

246 Conflict of interest

247 None.

248

249

250
251
252

Reference:

(1) Oecd.org. (2017). Obesity-Update-2017. [online] Available at https://www.oecd.org/els/health-systems/Obesity-Update-2017.pdf

(2) NIH. (2012).The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) [online] Available at: :http://www.obesityresearch.nih.gov. Updated December 2012.

(3) Moghaddam, A. A., Woodward, M., & Huxley, R. (2007). Obesity and Risk of Colorectal Cancer: A Meta-analysis of 31 Studies with 70,000 Events. Cancer Epidemiology Biomarkers & Prevention,16(12), 2533-2547.

(4) Calle, E. E., Rodriguez, C., Walker-Thurmond, K., & Thun, M. J. (2003). Overweight, Obesity, and Mortality from Cancer in a Prospectively Studied Cohort of U.S. Adults. New England Journal of Medicine,348(17), 1625-1638.

(5) McArdle C.S., McMillan D.C.,& Hole D.J. (2003). Male gender adversely affects survival following surgery for colorectal cancer. Br J Surg, 90:711–5.

(6) Quirt J.S, Nanji S, Wei X., Flemming J.A., &Booth C.M. (2017). Is there a sex effect in colon cancer? Disease characteristics, management, and outcomes in routine clinical practice. Current Oncology.;24(1):e15-e23.

(7) Almasaudi, A. S., McSorley, S. T., Edwards, C. A., & McMillan, D. C. (2017). The relationship between body mass index and short term postoperative outcomes in patients undergoing potentially curative surgery for colorectal cancer: A systematic review and meta-analysis. Critical Reviews in Oncology/Hematology, 121, 68–73.

(8) Weiss, C. A. (1999). Six Years of Surgical Wound Infection Surveillance at a Tertiary Care Center. Archives of Surgery,134(10), 1041.

(9) Horan, T. C., Gaynes, R. P., Martone, W. J., Jarvis, W. R., & Emori, T. G. (1992). CDC Definitions of Nosocomial Surgical Site Infections, 1992: A Modification of CDC

Definitions of Surgical Wound Infections. Infection Control and Hospital Epidemiology,13(10), 606-608.

(10) Dimick, J. B., Chen, S. L., Taheri, P. A., Henderson, W. G., Khuri, S. F., & Campbell, D. A. (2004). Hospital costs associated with surgical complications: A report from the private-sector National Surgical Quality Improvement Program. Journal of the American College of Surgeons,199(4), 531-537.

(11) Khuri, S. F., Henderson, W. G., Depalma, R. G., Mosca, C., Healey, N. A., & Kumbhani, D. J. (2005). Determinants of Long-Term Survival After Major Surgery and the Adverse Effect of Postoperative Complications. Transactions of the Meeting of the American Surgical Association,123(&NA;), 32-48.

(12) Jung, U., & Choi, M. (2014). Obesity and Its Metabolic Complications: The Role of Adipokines and the Relationship between Obesity, Inflammation, Insulin Resistance, Dyslipidemia and Nonalcoholic Fatty Liver Disease. International Journal of Molecular Sciences,15(4), 6184-6223.

(13) Makino, T., Shukla, P. J., Rubino, F., & Milsom, J. W. (2012). The Impact of Obesity on Perioperative Outcomes After Laparoscopic Colorectal Resection. Annals of Surgery,255(2), 228-236

(14) Balentine, C. J., Wilks, J., Robinson, C., Marshall, C., Anaya, D., Albo, D., & Berger, D. H. (2010). Obesity Increases Wound Complications in Rectal Cancer Surgery. Journal of Surgical Research, 163(1), 35-39.

(15) Murphy, T.K., Calle, E.E, Rodriguez C, Kahn H.S, &Thun, M.J. (2000). Body mass index and colon cancer mortality in a large prospective study. Am J Epidemiol 152, 847–854.

(16) Kabon, B., Nagele, A., Reddy, D., Eagon, C., Fleshman, J. W., Sessler, D. I., & Kurz, A. (2004). Obesity Decreases Perioperative Tissue Oxygenation. Anesthesiology,100(2), 274-280.

Table 1. Clinico-pathological characteristics, systemic inflammation, and complications following surgery for colorectal cancer (male/female, n=1039).

Characteristics	Male n 587 (%) (56)	Female 452 (44)	P (value)
Age (<65/65-74/>74)	206/233/148 (35/40/25)	168/152/132 (37/34/29)	0.698
BMI (18.5-24.99/ 25-29.99/30-34.9/ ≥35)	194/228/114/51 (33/39/19/9)	183/132/79/58 (41/29/17/13)	0.859
Smoking (no/yes)*	418/83 (83/17)	319/55 (85/15)	0.455
Year of surgery (1997-2007/2008-2016)	183/403 (31/69)	140/312 (31/69)	0.930
TNM stage (I/II/III/IIII)	127/230/190/22 (23/40/33/4)	89/192/144/13 (20/44/33/3)	0.954
Tumour site (colon/ rectum)	345/239 (59/41)	299/151 (66/34)	**0.015**
ASA grade (1/2/3/4)	107/253/171/22 (19/46/31/4)	87/191/141/11 (20/44/33/3)	0.713
Preop mGPS (0/1/2)	418/67/59 (77/12/11)	320/60/42 (76/14/10)	0.978
NLR > 5 (no, yes)	427/81 (84/16)	345/55 (86/14)	0.358
Laparoscopic (no/yes)	244/141 (63/37)	184/107 (63/37)	0.969
Operative time > 4 h (no/yes)*	213/126 (63/37)	191/74 (72/28)	**0.017**
POD3 GPS (0/1/2)	225/96/80 (56/24/20)	216/46/59 (67/14/18)	**0.032**

POD4 GPS (0/1/2)	265/61/61 (68/16/16)	231/26/44 (77/9/15)	0.099
Neoadjuvant therapy (no/yes)	493/71 (87/13)	381/57 (87/13)	0.842
Adjuvant therapy (no/yes)	364/135 (73/27)	284/110 (72/28)	0.774
Any complication (no/yes)	303/241 (56/44)	281/145 (66/34)	**≤0.001**
Non-infective complication(no/yes)	440/104 (81/19)	363/63 (85/15)	0.076
Infective complication (no/yes)	384/160 (71/29)	329/97 (77/23)	**0.020**
Surgical site infection (no/yes)	436/104 (81/19)	368/57 (87/13)	**0.016**
Wound infection (no/yes)	477/67 (88/12)	392/34 (92/8)	**0.028**
Anastomotic leak (no/yes)	511/33 (94/6)	412/14 (98/3)	**0.046**

Chi square test for linear association. Data are expressed n (%)
Pre-op mGPS: preoperative modified Glasgow prognostic score
Pre-op NLR: preoperative neutrophil/lymphocyte ratio
POD: Post Operative Day
* Missing value

Table 2. The relationship between BMI, clinicopathological characteristic and postoperative complications in male patients with colorectal cancer (n=587).

Characteristics	Total Patients	BMI				P (value)
	n (%)	18.5-24.99 194 (33)	25-29.99 228 (39)	30-34.99 114 (19)	≥35 51 (9)	
Age (65,65-74, >75)	206/233/148 (35/40/25)	66/63/65 (34/33/33)	82/88/58 (36/3925)	36/60/18/114 (32/53/16)	22/22/7 (43/43/14)	**0.010**
Year of surgery (1997-2007/2008-2016)	183/204 (31/69)	66/127 (34/66)	83/145 (36/64)	22/92 (19/81)	12/39 (23/77)	**0.009**
TNM stage (I/II/III/IIII)	127/230/190/22 (23/40/33/4)	37/90//53/7 (20/48/28/4)	45/83/85/8 (20/38/39/4)	32/38/35/6 (29/34/31/5)	13/19/17/1 (26/38/34/2)	0.672
Smoking (no/yes)	418/83 (83/17)	128/38 (77/23)	161/33 (83/17)	92/12 (89/11)	37/0 (100/0)	**<0.001**
Tumour site (colon/ rectum)	345/239 (59/41)	109/84 (57/43)	136/91 (60/40)	69/45 (60/40)	31/19 (62/38)	0.386
Preop mGPS(0/1/2)	418/67/59 (77/12/11)	119/29/27 (68/17/15)	178/18/20 (82/8/10)	86/14/6 (81/13/6)	35/6/6 (74/13/13)	**0.040**
NLR > 5 (no, yes)	427/81 (84/16)	126/39 (76/24)	165/27 (86/14)	94/12 (89/11)	42/3 (93/7)	**<0.001**
ASA grade (1/2/3/4)	107/253/171/22 (19/46/31/4)	34/82/61/7 (19/45/33/4)	54/90/61/8 (25/42/29/4)	13/59/29/6 (12/55/27/6)	6/22/20/1 (12/45/41/2)	0.393
Laparoscopic (no/yes)*	244/141 (63/37)	82/35 (70/30)	81/58 (58/42)	56/35 (62/38)	25/13 (66/34)	0.379

Operative time > 4 h (no/yes)*	213/126 (63/37)	64/38 (63/37)	75/50 (60/40)	54/28 (66/34)	20/10 (67/33)	0.561
PoGPS-D3(0/1/2)	225/96/80 (56/24/20)	84/16/35 (62/12/26)	88/35/22 (61/24/15)	40/30/14 (48/36/17)	13/15/9 (35/41/24)	0.125
PoGPS-D4(0/1/2)	265/61/61 (68/16/16)	85/13/25 (69/11/20)	110/17/20 (75/12/14)	47/21/11 (59/27/14)	23/10/5 (61/26/13)	0.730
Neoadjuvant therapy (no/yes)	493/71 (87/13)	151/34 (82/18)	195/25 (89/11)	103/8 (93/7)	44/4 (92/8)	**0.005**
Adjuvant therapy (no/yes)	364/135 (73/27)	130/38 (77/23)	141/59 (70/30)	63/25 (72/28)	30/13 (70/30)	0.216
Any complication (no/yes)	303/241 (56/44)	103/77 (57/43)	121/88 (56/42)	55/53 (51/49)	24/23 (51/49)	0.258
Non-infective complication(no/yes)	440/104 (81/19)	148/32 (82/18)	170/39 (81/19)	85/23 (79/21)	37/10 (79/21)	0428.
Infective complication(no/yes)	384/160 (71/29)	131/49 (73/27)	149/60 (71/29)	73/35 (68/32)	31/16 (66/34)	0.246
Surgical site infection (no/yes)	436/104 (81/19)	157/22 (88/12)	167/41 (80/20)	79/28 (74/26)	33/13 (72/28)	**<0.001**
Wound infection (no/yes)	477/67 (88/12)	168/12 (93/7)	187/22 (90/10)	86/22 (8/20)	36/11 (77/23)	**<0.001**
Anastomotic leak (no/yes)	511/33 (94/6)	173/7 (96/4)	192/17 (92/8)	103/5 (95/5)	43/4 (92/8)	0.370

Table 3. Relationship between surgical site infection, BMI and associated clinic-pathological characteristics in male patients with colorectal cancer. (n=587).

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
BMI	1.45(1.16-1.81)	**≤0.001**	1.42(1.13-1.78)	**0.002**
Age	0.76(0.57-1.00)	**0.055**	-	0.107
Smoking	0.98(0.50-1.93)	0.959	-	-
Year of surgery	1.22(0.76-1.94)	0.413	-	-
Neoadjuvant therapy	0.165(0.90-3.01)	0.104	-	-
Pre-op mGPS	1.03(0.75-1.42)	0.851	-	-
NLR>5	0.90(0.48-1.69)	0.747	-	-

Binary logistic regression model

Table 4. The relationship between BMI, clinicopathological characteristic and postoperative complications in female patients with colorectal cancer (n=452).

Characteristics	Total Patients	BMI				P (value)
	n (%)	18.5-24.99 183 (41%)	25-29.99 132 (29%)	30-34.99 79 (17%)	≥35 58 (13%)	
Age (65,65-74, >75)	168/152/132 (37/34/29)	58/60/65 (32/33/35)	49/49/34 (37/37/26)	30/29/20 (38/37/25)	31/14/13 (63/24/22)	**0.004**
Year of surgery (1997-2007/2008-2016)	140/312 (31/69)	73/110 (40/60)	42/90 (32/68)	21/58 (27/74)	4/54 (7/93)	**<0.001**
Smoking (no/yes)	319/55 (85/15)	121/19 (86/14)	93/23 (80/20)	57/8 (88/12)	48/5 (91/9)	0.441
TNM stage (I/II/III/IIII)	89/192/144/13 (20/44/33/3)	29/95/51/4 (17/53/29/2)	29/40/52/4 (23/32/42/3)	19/32/25/1 (25/42/32/1)	12/25/16/4 (21/44/28/7)	0.952
Tumour site (colon/ rectum)	229/151 (66/34)	120/63 (66/34)	87/44 (66/34)	52/26 (67/33)	40/18 (69/31)	0.655
Preop mGPS (0/1/2)	320/60/42 (76/14/10)	129/21/23 (75/12/13)	95/17/12 (77/14/10)	56/14/3 (77/19/4)	40/8/4 (77/15/8)	0.239
NLR > 5 (no, yes)	345/55 (86/14)	127/32 (80/20)	106/13 (89/11)	62/7 (90/10)	50/33 (94/6)	**0.004**
ASA grade (1/2/3/4)	87/191/141/11 (20/44/33/3)	46/67/54/5 (27/39/31/3)	25/60/40/1 (20/48/32/1)	8/38/25/4 (11/51/33/5)	8/26/22/1 (14/46/39/2)	**0.033**
Laparoscopic (no/yes)*	184/107 (63/37)	77/28 (73/27)	48/35 (58/42)	32/23 (58/42)	27/21 (56/44)	**0.025**

Operative time > 4 h (no/yes)*	191/74 (72/28)	70/19 (79/21)	56/24 (70/30)	36/14 (72/28)	29/17 (63/37)	0.074
PoGPS-D3(0/1/2)	216/46/59 (67/14/18)	86/10/25 (71/8/21)	66/15/12 (71/16/13)	36/9/12 (63/16/21)	28/12/10 (56/24/20)	0.221
PoGPS-D4(0/1/2)	231/26/44 (77/9/15)	87/4/16 (81/4/15)	80/7/9 (83/7/9)	42/4/8 (78/7/15)	22/11/11 (50/25/25)	**0.006**
Neoadjuvant therapy (no/yes)	381/57 (87/13)	150/30 (83/17)	110/15 (88/12)	70/7 (91/9)	51/5 (91/9)	0.055
Adjuvant therapy (no/yes)	284/110 (72/28)	130/34 (79/21)	71/45 (61/39)	52/16 (76/24)	31/15 (67/33)	0.152
Any complication (no/yes)	281/145 (66/34)	119/53 (69/31)	84/43 (66/34)	49/25 (66/34)	29/24 (55/45)	0.089
Non-infective complication(no/yes)	363/63 (85/15)	148/24 (86/14)	104/23 (82/18)	64/10 (86/14)	47/6 (89/11)	0.676
Infective complication(no/yes)	329/97 (77/23)	138/34 (80/20)	102/25 (80/20)	56/18 (76/24)	33/20 (62/38)	**0.014**
Surgical site infection (no/yes)	368/57 (86/14)	154/18 (90/10)	108/19 (85/15)	66/7 (90/10)	40/13 (75/25)	0.054
Wound infection (no/yes)	392/34 (92/8)	162/10 (94/6)	120/7 (94/6)	68/6 (92/8)	42/11 (79/21)	**0.003**
Anastomotic leak (no/yes)	412/14 (98/3)	167/5 (97/5)	122/5 (96/4)	73/1 (99/1)	50/3 (94/6)	0.649

Table 5. Relationship between surgical site infection, BMI and associated clinic-pathological characteristics in female patients with colorectal cancer (n=452).

Variable	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
BMI	1.29 (0.99-1.67)	**0.055**	-	0.274
Age	0.79 (0.55-1.11)	0.180	-	-
Year of surgery	1.72(0.89-3.31)	0.105	-	-
ASA grade	1.01(0.70-1.46)	0.944	-	-
NLR>5	2.79(1.39-5.61)	**0.004**	2.92(1.09-7.81)	**0.033**
Laparoscopic	0.32(0.14-0.72)	**0.006**	-	0.105
POD 4 GPS	2.03(1.42-2.92)	**≤0.001**	2.22(1.47-3.34)	**<0.001**