

## The Effect of Obesity on Outcomes Following Colorectal Surgery

How P\*, Choo S, Koshy R, Benziger H

Colorectal Unit, Queen Elizabeth Queen Mother Hospital, Margate, UK

\*Corresponding Author: How P, Colorectal Unit, Queen Elizabeth Queen Mother Hospital, Margate, UK.

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### Abstract

**Background:** Obesity has become a major health concern in the developed world and the obese patient presents a number of challenges to the modern day surgeon. This review looks at how obesity affects outcomes in patients undergoing colorectal surgery.

**Methods:** EMBASE, MEDLINE and PUBMED databases were searched for relevant studies from 2009 onwards with the emphasis on those reporting specific outcomes.

**Results:** There is strong evidence that obesity significantly increases the risk of surgical site infections (SSIs) and thromboembolic complications following colorectal surgery. Obesity is associated with greater blood loss, longer operating times and higher conversion rates and may increase the risk of wound disruption, incisional and parastomal herniae. There is mixed data with respect to cardiopulmonary complications, anastomotic leak and length of hospital stay.

**Conclusion:** Obesity has an adverse effect on outcomes after colorectal surgery. Many studies include a heterogenous study population with respect to surgery which can limit interpretation. It is recommended that future studies focus on more specific patient groups and use alternative measures of visceral and peripheral obesity besides BMI.

**Keywords:** Obesity; Colorectal Surgery; BMI

### Introduction

Obesity has become a major public health concern in the developed world. Obesity prevalence has rapidly increased over the last 40 years with 39% of adults being classified as overweight or obese in 2016 [1]. Obesity has traditionally been measured by body mass index (BMI) which is calculated as: bodyweight (kg)/height (m) [2].

A BMI of 18.5 to 24.9 is classified as normal and that between 25 - 29.9 as overweight. BMI 30 - 34.9 represents class 1 obesity, 35 - 39.9 class 2 and  $\geq 40$  class 3.

Over the last 20 - 30 years, there is an increasingly strong body of evidence for obesity as an independent risk factor for a broad range of cancers including oesophagus, pancreas and colon [2]. One proposed mechanism for this is that obesity and more specifically, visceral fat, has an effect on hormones such as insulin and IGF which are implicated in oncogenesis [3].

Given the increasing prevalence of obesity and risk of cancer that it confers, it is expected that such patients will constitute a significant proportion of the colorectal surgeon's workload. However, current data regarding the effects of obesity are varied and often inconsistent. Surgeon and patient factors play a decisive role in outcome. The aim of this review was to provide an up to date analysis of the available data regarding the impact of obesity on outcomes following major colorectal surgery.

### Methods

EMBASE, MEDLINE and PUBMED databases were searched using the terms 'obesity' and 'colorectal surgery'.

When analysing specific outcomes, duplication of data was avoided by including data from a single unit only once and excluding review articles or meta-analyses. Our main focus was on well-designed cohort studies or randomized controlled trial (RCT) data when available.

Since our intention was to provide a modern review, and to prevent potential repetition of previous reviews on a similar topic, we omitted studies published before 2009 for our analyses.

### Surgical site infections

Obesity is a well-established risk factor for surgical site infections (SSIs) following a broad range of abdominal procedures that includes colorectal surgery [4].

The pathophysiology underlying this is considered to be multifactorial with an increase in subcutaneous fat predisposing to impaired angiogenesis, chronic low grade inflammation and poor tissue oxygenation. Surgical site infections carry significant implications for the patient as they can cause pain, wound breakdown and prolonged hospital stay.

Furthermore, colorectal surgery confers a higher risk of infection as bowel is commonly entered exposing subcutaneous tissue to intestinal bacteria.

A recent US based retrospective cohort study of 74,891 patients undergoing elective colorectal surgery demonstrated that obese patients experienced incremental odds of surgical site infection depending on class of obesity compared to normal weight subjects [5]. The authors reported odds ratios of 1.5, 1.9 and 2.1 for classes 1,2 and 3 respectively and observed the highest rates of wound disruption, sepsis and urinary tract infections in obesity class 3 patients. A similar UK based study of 3495 patients undergoing large bowel surgery across 206 hospitals reported an odds ratio of 2.99 for SSI in Obesity class 2 patients [6].

Another cohort study [7] reported on 1737 patients undergoing colectomy for diverticulitis and identified obesity (BMI > 30) as a predictor for SSI on univariate analysis. In combination with other patient and surgical factors, the authors were able to risk stratify patients by developing a scale (Prediction and Enaction of Prevention Treatments Trigger) with the aim of targeting high risk groups with SSI prevention bundles.

Despite its widespread use in classifying obesity, the BMI is limited in being able to distinguish fat from muscle mass, and visceral obesity from peripheral or subcutaneous fat. It is the latter which is considered to be the significant risk factor for SSI. Fujii, *et al.* [8] compared BMI with the thickness of subcutaneous fat (TSF) in predicting SSI in 152 patients who underwent elective colorectal resection. TSF was measured preoperatively using computed tomography (CT). Interestingly, the authors found that whilst both parameters were significant on univariate analysis, only TSF retained its significance on multivariate analysis. In contrast, visceral fat volume did not prove predictive for SSI in a study of 79 patients [9].

As a result of SSIs, obesity has a significant economic impact. In an analysis of 7020 colectomy patients, Wick, *et al.* [10] found obesity to be an independent risk factor for SSI with an increased risk of 60%. Prolonged hospital stay as a consequence of infection was found to increase the colectomy cost by a mean of \$17,324.

The most recent evidence would suggest that obesity is an important risk factor for SSI after colorectal surgery. As a result, some authors have recommended additional measures such as negative pressure wound therapy and skin glue to complement current guidelines intended to minimize SSIs.

### Cardiopulmonary complications

Obesity increases chest wall resistance, reduces lung compliance and is associated with reduced tidal volume, vital capacity, total lung capacity and functional residual capacity [11]. The effect of this is to predispose the patient to post-operative atelectasis, hypoxia and pneumonia. Furthermore, obesity and the associated metabolic syndrome increases the risk of post-operative arrhythmias, heart failure and cardiac arrest [12].

Recent data relating specifically to colorectal surgery is limited but important given the development of minimally invasive techniques and the widespread adoption of ERAS (Enhanced Recovery after Surgery) programmes.

In a retrospective analysis of 1298 patients undergoing colorectal procedures between 2011 and 2017, Jurt., *et al.* [13] identified minimally invasive surgery and compliance with ERAS protocol as protective factors against post-operative pulmonary complications (PPC). Independent risk factors for PPC were emergency surgery, blood loss of  $\geq 200$  mls and ASA  $\geq 3$ . Obesity did not prove significant on multivariate analysis though subgroup analysis on those undergoing open procedures only was not performed.

In a similar study, Hancock., *et al.* [14] performed a retrospective analysis of 101 patients from a prospectively collected ERAS database who had undergone elective colorectal surgery within a 12 month period from 2015 to 2016. The authors found no significant association between BMI and respiratory complications. However, as only 7 (6.9%) patients developed respiratory complications, this study may be underpowered to detect a difference.

Data pertaining to cardiac complications is mixed. In a retrospective analysis of 310,208 NSQIP (National Surgical Quality Improvement Program) patients, Glance., *et al.* [15] did not find a difference in the incidence of adverse cardiac events (myocardial infarction or cardiac arrest) between patients with a normal BMI (18.5 - 24) and those who were overweight (BMI 25 - 29) or obese (BMI > 30). However, further subgroup analysis of patients with the modified metabolic syndrome (overweight, obese or morbidly obese and central obesity, hypertension, hyperglycaemia, dyslipidaemia and/or prothrombotic states) had a 2 - 2.5 fold higher risk of adverse cardiac events compared to normal weight patients. This risk was stratified according to BMI and obesity classification.

Watanabe., *et al.* [16] investigated predictive factors for post-op complications in 33,411 Japanese patients undergoing low anterior resection (LAR) from a national database. Amongst the complications of interest were pneumonia and cardiac events; BMI did not prove significant for either though cardiac complications occurred in only a very small number of cases (0.3%). It is also not known how many overweight (BMI > 26) and obese (BMI > 30) patients were included in this study; the lower prevalence of obesity in Japan would make any potential difference difficult to detect.

### Thromboembolic complications in colorectal surgery

Thromboembolic complications encompass both Deep Vein Thromboses (DVT) and Pulmonary Embolisms (PE). Colorectal Surgery has a high incidence of thromboembolic complications because it is commonly performed for malignancies and inflammatory bowel disease [17]. Furthermore, the intraoperative lithotomy positioning, pelvic dissection and prolonged operative times are thought to confer a greater risk of thrombosis. Without the appropriate thromboembolic prophylaxis, the rates of postoperative DVT and PE have been shown to be as high as 40% and 5% respectively for colorectal surgery [18].

There is an increasingly significant body of evidence supporting the view that obesity increases the risk of thromboembolic events in patients undergoing colorectal procedures.

One retrospective study [19] examined 219,477 patients from the American College of Surgeons National Surgical Quality Improvement Project (ACS NSQIP) database that underwent colorectal surgery between 2005 and 2013. Following multivariate analysis, obesity (Adjusted Odds Ratio, AOR 1.37,  $P < 0.01$ ) was one of the factors associated with an increased risk of post-discharge thromboembolic events in addition to chronic steroid use (AOR 1.91,  $P < 0.01$ ), open surgery (AOR 1.36,  $P < 0.01$ ), stage 4 colorectal cancer (AOR 1.4  $P = 0.03$ ) and age greater than 70 (AOR 12.34,  $P < 0.01$ ). Similarly, Fleming., *et al.* [20] evaluated post discharge venous thromboembolic incidence in 52,555 patients that had undergone colon or rectum resection between 2005 and 2008. Obesity (BMI > 30 kg/m<sup>2</sup>) was reported to be one of the independent predictors together with preoperative steroid use, bleeding disorders, ASA grade III and postoperative infection.

Buchberg, *et al.* [21] investigated the incidence of thromboembolism after laparoscopic versus open colorectal surgery in 149,304 patients over a 60-month period using data from a national database and found that obese patients who underwent both laparoscopic and open colorectal surgery had a significantly higher risk of thromboembolic events with odds ratios of 2.3 and 1.9 respectively.

Esemuede, *et al.* [22] examined 130,415 patients in the NSQIP database from 2006 to 2011 and compared obese (BMI > 30) to non-obese (BMI < 30) patients who underwent colorectal resections. It was found that obese patients, regardless of the presence or absence of co-morbidities, more frequently had pulmonary embolisms suggesting that obesity should be included as an independent determinant of operative severity, quality and re-imburement after surgery.

Merkow, *et al.* [23] utilised data from the ACS NSQIP database and identified a total of 3,202 patients who underwent colectomy for malignancy. The results approximated those previous studies looking at patients undergoing colorectal procedures, suggesting that morbidly obese (BMI  $\geq 35$  kg/m<sup>2</sup>) patients have a higher risk of pulmonary embolisms (OR 6.98) than overweight or non-obese patients despite no difference in the incidence of deep vein thrombosis. This is surprising but could be explained by the largely non-specific, subclinical presentation of DVT and that obesity may impede its early diagnosis [24].

Recent analyses of both single centre and multicentre large sample studies have reported that thromboembolic events have been observed to be significantly higher in the obese population [19-21] compared to non-obese patients. It is postulated that obesity leads to coagulation abnormalities and abnormal platelet activation which significantly increases the risk of thromboembolism. In combination with the inherent risk associated with colorectal surgery, it is easy to see why obese patients being treated for colorectal cancer, diverticular and inflammatory bowel disease are amongst the most vulnerable patients. Recent guidelines regarding risk stratification and thromboprophylaxis have been introduced to help minimize morbidity and mortality.

### Anastomotic leak

Anastomotic leak (AL) is a potentially devastating complication following restorative colorectal surgery with significant associated morbidity and mortality. It has a reported incidence of up to 19% [25] and represents an interplay between patient and technical surgical factors that increase the risk of AL. Male sex, preoperative radiotherapy, low level anastomosis, steroid and immunosuppressant therapy are widely acknowledged as established risk factors [26]. What is less clear however is the impact of obesity on AL given the recent advances in minimally invasive surgery.

In a recent retrospective analysis of 225 patients undergoing restorative resection for colorectal cancer, Adamova, *et al.* [27] did not observe any statistically significant difference in AL when matched for age, sex, co-morbidities and cancer stage. A larger case series of 1464 patients [28] did demonstrate increased rates of surgical complications including anastomotic leakage with elevated BMI. Interestingly, the increased risk of AL was associated with a BMI of > 35 for colon cancer and > 30 for rectal cancer highlighting the increased risk conferred by pelvic surgery. The authors also found that conversion from laparoscopic to open surgery was 1.9 times more likely in obese patients with colon cancer and 4.1 times more likely in obese patients with rectal cancer. This is important as conversion often results from a technically challenging operation - the larger amount of visceral fat encountered in obese patients can make surgical planes difficult to identify and may hinder the construction of a well perfused tension free anastomosis. It is not clear from this study how many of these obese patients were diabetic; the associated microvascular disease with this condition may further increase the risk of AL.

The mixed evidence for obesity as an independent risk factor for AL can be further highlighted by two similar sized studies originating from Japan and the UK. In a single centre study of 1194 patients undergoing laparoscopic resection for colorectal cancer in Japan, Akiyoshi, *et al.* [29] reported a higher rate of AL in obese class 2 patients (BMI  $\geq 30$ ) than in non-obese and obese class 1 patients ( $25 \leq$  BMI < 30) and that BMI in the obese class 2 range was an independent predictive factor for developing AL on multivariate analysis. Blood loss and operating times were also longer in the obese groups. By contrast, a retrospective analysis of 1386 patients from three UK centres

[30] failed to show a difference in AL rates between morbidly obese (BMI > 35), obese ( $30 \leq \text{BMI} < 35$ ) and non-obese patients (BMI < 30) despite similarly longer operating times and greater blood loss in the obese groups. The increased technical difficulty encountered in these obese patients did not translate into worse short-term outcomes unlike their Japanese counterparts. The difference in outcomes observed in these two studies may relate to the contrasting study populations. A comparatively smaller caseload of obese patients for the Japanese surgeon may impart a longer learning curve.

Statistically significant associations between high BMI and AL have been reported in similarly large population studies for both rectal [31] and colonic resections [32] where data was collected from a high volume specialized tertiary centre and a prospective multicentre study respectively. Interestingly, in a subgroup analysis of patients undergoing elective right hemicolectomy, the same authors did not demonstrate a relationship between obesity and AL [33] suggesting a stronger association with left sided resections.

Given the above, it would perhaps be better to look at other indices of obesity besides BMI which has its limitations as described earlier. In a prospective multicentre study of 1349 patients, Kartheuser, *et al.* [34] examined the effect of waist circumference (WC) and waist/hip ratio (WHR) on postoperative outcomes in patients undergoing elective colorectal surgery. They found that increasing WHR significantly increased the risk of AL (OR = 13.7, RR = 3.3) and was predictive of AL upon multivariate analysis whereas BMI did not prove significant. The importance of fat distribution as opposed to BMI as a marker of obesity is further underlined by the findings of Watanabe, *et al.* [35]. In this Japanese study of 338 patients, the authors investigated the comparative impact of visceral obesity (VO) and BMI on surgical outcomes of laparoscopic surgery for colon cancer. Whilst both independently predicted the incidence of overall postoperative complications, there was a stronger correlation between VO and AL than high BMI. The reported association of VO with greater postoperative complications may be explained by the increased postoperative inflammatory response observed in patients with a high visceral to subcutaneous fat ratio [36].

### Operating time and length of hospital stay

Obese patients represent a greater technical challenge than non-obese patients on account of the greater amount of fat, both subcutaneous and visceral that can significantly hinder access and impede tissue plane visualization. Prolonged operating times as a result of this may also impact blood loss, conversion rates and length of hospital stay.

Bege, *et al.* [37] reported longer operating times and higher conversion rates for obese patients (BMI  $\geq 30$ ) than non-obese patients undergoing laparoscopic resection for rectal cancer. A more recent high powered national study of 45,362 patients in the US [38] did also report BMI as an independent predictor of operating time across elective colorectal procedures. Open ileocolic resections and laparoscopic low pelvic anastomoses took on average 17.8 and 56.6 minutes longer respectively in morbidly obese patients (BMI > 35), highlighting the additional challenges of pelvic surgery. However, this study did not report on associated blood loss or conversion rates and the study population included a heterogeneous patient profile: open and laparoscopic ileocolic resections, partial colectomies and low pelvic anastomoses. Since laparoscopic surgery is now considered feasible and safe with better cosmesis and faster patient recovery, it is perhaps more important to focus on relevant studies of patients undergoing laparoscopic resections. In a study of 626 patients undergoing laparoscopic colorectal resection for IBD, Krane, *et al.* [39] did demonstrate a positive correlation between obesity and longer operating times, greater blood loss and increased conversion rates though this did not impact 30 day postoperative morbidity and mortality. Whilst not reported in this study, prolonged post-operative ileus (PPOI) leading to prolonged hospital stay has been linked to obesity [40] though there is evidence to suggest that robotic surgery for rectal cancer can accelerate postoperative recovery in obese patients and can even lead to better short term outcomes despite a longer operating time when compared to laparoscopy [41].

In Japan, where obesity is less prevalent but nevertheless increasing, mixed results have been reported. Despite demonstrating a longer operating time of approximately 49 minutes in obese (BMI  $\geq 25$ ) versus non-obese patients (BMI < 25) undergoing laparoscopic

colorectal surgery, conversion rates, blood loss, lymph node yield and hospital stay were comparable [42]. It is difficult to draw meaningful conclusions however from this single centre study given its small study population (n = 65). In contrast, an earlier Japanese study of 1194 patients [29] did show obesity to not only increase mean operating time but also estimated blood loss and postoperative complications including anastomotic leak.

### Wound disruption, incisional and parastomal hernia

Abdominal wound disruption (AWD) is a potentially severe complication of colorectal surgery and has a reported incidence of 0.4% to 3.5%, with mortality rates as high as 45% [43]. It is defined as a spontaneous reopening of a previously surgically closed (midline) wound that occurs within 30 days after the index operation [44]. It has various synonyms in the literature including abdominal wound dehiscence, fascial dehiscence, or burst abdomen.

In a study of 164,297 patients from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) undergoing resection between 2005 and 2013, 2073 (1.3%) developed wound disruption with obesity reported as a risk factor with an adjusted odds ratio (AOR) of 1.57 (P < 0.01) [45]. Interestingly, the same study identified wound infection as conferring the highest risk of AWD with an AOR of 4.11 (P < 0.01). This is not surprising given our previous discussion regarding the risk of SSI and obesity. The authors did also demonstrate a lower overall risk of wound disruption in patients undergoing laparoscopic surgery compared to open surgery though a subgroup analysis of laparoscopic obese versus open obese patients was not performed. Whilst it would appear logical in assuming that the lower risk of AWD conferred by laparoscopic surgery would be even more telling in obese patients, one must bear in mind the increased operating times and conversion rates associated with obese patients [34]. In this same study, operation length greater than 3 hours was another risk factor for AWD.

Interestingly, in a related study of 690 patients derived from the same database (NSQIP) from 2006 to 2012, obesity was not found to be predictive for AWD [46]. Only male gender, absence of an SSI bundle and hypoalbuminaemia were reported as independent predictors for AWD after elective colorectal resections. It is difficult to explain why obesity was significant in one study and not in the other given their similarity. One reason could be that the study by Moghadamyeghaneh, *et al.* [45] included both elective and emergency operations whilst Gachabayov, *et al.* [46] included elective patients only. It is expected that a larger proportion of patients admitted as an emergency would undergo open surgery as opposed to laparoscopic procedures in elective surgery, thereby increasing the risk of wound complications in obese patients.

Incisional hernia is another common surgical complication with considerable morbidity including reduced quality of life and significant risk of incarceration or strangulation necessitating urgent repair [47]. Obesity is an especially important risk factor for incisional hernia as it is strongly associated with hernia development [48]. The link between obesity and incisional hernia is believed to be due to increased abdominal wall tension and a direct link between obesity and increased intra-abdominal pressure.

As a result of the links between obesity and incisional hernia, there is growing interest in developing preventative strategies. In a study of 72 patients where 41 (57%) were obese (BMI >30), Hidalgo, *et al.* [49] reported favourable long term outcomes with the prophylactic placement of a preperitoneal prolene mesh in patients undergoing laparotomy. Indeed, none of the patients developed incisional hernia or significant infective complication requiring mesh removal. Whilst encouraging, the lack of a control group, small sample size and variable follow up time limits any meaningful conclusions.

Stoma formation in obese patients is particularly challenging because of the increased colonic mobilization required in order for the stoma to traverse a thick abdominal wall. As a result, there is an increased risk of stoma related complications including stenosis, retraction, ischaemia and parastomal hernia. Pre-operative stoma site marking represents an additional challenge due to the often pendulous

nature of the abdomen and the difficulty with which the patient can visualize the stoma. In a retrospective study of 202 consecutive patients receiving intestinal stomas following colorectal surgery, Harilingham, *et al.* [50] found that obesity (BMI >30) was a predictor for stomal complications including retraction and parastomal hernia.

In contrast to the formentioned studies originating from the West, a retrospective analysis of 690 Korean patients undergoing colorectal surgery [51] did not identify obesity as a risk factor for either incisional or parastomal herniae. However, given that the overall rate of incisional and parastomal herniae were only 2% (14/690) and 6.7% (7/105) respectively, it is possible that this represents type 2 error.

### Conclusions

From our review of the literature, there is strong evidence in support of obesity as a significant risk factor for wound infections and thromboembolic complications after colorectal surgery. The data is mixed however with respect to cardiopulmonary complications, anastomotic leak, operating time and length of stay, wound disruption and herniae. These inconsistent findings may be attributable to both the heterogenous nature of study populations (East Vs West) and the type of surgery performed (elective Vs emergency, open Vs laparoscopic). Furthermore, there is likely to be significant variation in patient selection with respect to a minimally invasive approach and the adoption of enhanced recovery programmes. Both of these would impact heavily upon blood loss, operating times, conversion rates, overall morbidity and length of hospital stay.

Although not entirely consistent, there is enough evidence to suggest that obesity increases operating times, blood loss and conversion rates whilst not necessarily impacting length of stay. There is also enough evidence to suggest that obesity increases the risk of developing abdominal wall complications in the form of wound disruption, incisional and parastomal herniae.

Whilst the vast majority of the literature quantify obesity according to BMI, there is increasing evidence that other indices such as subcutaneous or visceral fat recorded from pre-operative CT or the waist to hip ratio (WHR) are more reliable. However, there remains a lack of high powered studies that use these parameters which is understandable given the greater accessibility of recording BMI. Our focus during this review were studies that investigated or reported specific complications following colorectal surgery; single centre studies with limited sample sizes reporting upon overall morbidity and mortality were largely excluded from our commentary. It is hoped that future obesity related studies may give more meaningful information by investigating specific complications within larger multicentre studies or by more targeted analyses of national registries. Most of the studies included in our review are retrospective or case controlled and susceptible therefore to selection bias with the intention of demonstrating a positive correlation. Though we have done our best to present a balanced view of the data available, publication bias remains an important factor and it is not known how many non-significant associations of obesity were never published.

Despite these limitations, it is clear from our review that the obese patient presents a unique set of challenges to the colorectal surgeon who can expect to encounter these with increasing frequency in the developed world. Perioperative care in the obese patient should include weight loss, strength training, psychological and nutritional counselling, incentive spirometry, early mobilization and chest physiotherapy, close post-operative observation of wounds and extended thromboprophylaxis. Further outpatient follow up should look for abdominal wall complications that would benefit from timely surgical intervention. It is hoped that in addition to improvements in surgical technique and strategy, patient tailored prehabilitation and enhanced recovery programmes will help significantly reduce postoperative morbidity.

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