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Retrospective Study

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Effect of obesity on post-operative outcomes following colorectal cancer surgery

Mao D *et al.* Post-operative outcomes following CRC in obese

Abstract

BACKGROUND

Colorectal cancer (CRC) resection is now undertaken in an increasing number of obese patients. Existing studies have yet to reach a consensus as to whether obesity affects post-operative outcomes following CRC surgery.

AIM

To evaluate the post-operative outcomes of obese patients following CRC resection, as well as determine the post-operative outcomes of obese patients in the subgroup undergoing laparoscopic surgery.

METHODS

Six-hundred and fifteen CRC patients who underwent surgery at the Prince Charles Hospital between January 2010 and December 2020 were categorised into two groups based on body mass index (BMI): Obese [BMI ≥ 30 , $n = 182$ (29.6%)] and non-obese [BMI < 30 , $n = 433$ (70.4%)]. Demographics, co-morbidities, surgical features and post-operative outcomes were compared between both groups. Post-operative outcomes were also compared between both groups in the subgroup of patients undergoing laparoscopic surgery [($n = 472$: BMI ≥ 30 , $n = 336$ (71.2%); BMI < 30 : $n = 136$ (28.8%)].

RESULTS

Obese patients had a higher burden of cardiac (73.1% *vs* 56.8%, $P < 0.001$) and respiratory co-morbidities (37.4% *vs* 26.8%, $P = 0.01$). Obese patients were also more likely to undergo conversion to an open procedure (12.8% *vs* 5.1%, $P = 0.002$), however did not experience more post-operative complications (51.6% *vs* 44.1%, $P = 0.06$) or high-grade complications (19.2% *vs* 14.1%, $P = 0.11$). In the laparoscopic subgroup however, obesity was associated with a higher prevalence of post-operative complications (47.8% *vs* 39.3%, $P = 0.05$) but not high-grade complications (17.6% *vs* 11.0%, $P = 0.07$).

CONCLUSION

Surgical resection of CRC in obese individuals is safe. A higher prevalence of post-operative complications in obese patients appears to only be in the context of laparoscopic surgery.

Key Words: Colorectal cancer; Obesity; Body mass index; Post-operative outcomes; Clavien-Dindo

Mao D, Flynn DE, Yerkovich S, Tran K, Gurunathan U, Chandrasegaram MD. Effect of obesity on post-operative outcomes following colorectal cancer surgery. *World J Gastrointest Oncol* 2022; In press

Core Tip: This is a retrospective study to assess the post-operative outcomes of obese patients undergoing colorectal cancer (CRC) resection. Obesity was defined as having a body mass index (BMI) of 30 kg/cm² or greater. Despite having a greater burden of cardiovascular and respiratory co-morbidities and an increased rate of conversion to open surgery, obese patients who underwent CRC resection were found to have equitable post-operative outcomes when compared to those with a normal BMI (< 30 kg/cm²). There were no differences in the severity of complications, length of stay, or mortality rates between both groups. Post-operative outcomes were also compared between obese and non-obese patients in the subgroup undergoing laparoscopic and laparoscopic-assisted surgery. Obese patients in this subgroup had a higher prevalence of post-operative complications, however were not at an increased likelihood of experiencing high-grade complications. CRC surgery in obese individuals is generally safe, with caution advised if a laparoscopic approach is planned.

INTRODUCTION

Colorectal cancer (CRC) contributes substantially to the healthcare burden worldwide^[1], and is the fourth most commonly diagnosed malignancy and second most common cause of cancer-related death in Australia^[2]. Obesity is a rising global pandemic associated with systemic disease and poor health outcomes^[3]. Body mass index (BMI) is an overall measure of total body fat, and is an easily calculable and accepted surrogate marker of obesity^[4]. The World Health Organization (WHO) defines obesity in adults as a BMI of 30 kg/cm² or greater^[5].

The increasing prevalence of obesity is of particular concern to colorectal surgeons, as it is not only implicated in the pathogenesis of CRC^[6], but also may have an impact on post-operative outcomes. However, with several studies reporting inconsistent findings^[7-9], there remains no consensus. The Clavien-Dindo Classification is a standardized system of grading post-operative complications, ranging from grade I (minor events) to grade V (death)^[10]. With objective criteria, it is a highly reproducible method of grading post-operative complications and is validated across several surgical disciplines, including colorectal surgery^[11].

In this study, we conducted a retrospective cohort study with an aim to outline and compare the clinical characteristics of obese and non-obese patients undergoing surgical resection of CRC at our institution, as well as evaluate the impact of obesity on post-operative outcomes using the Clavien-Dindo Classification of Surgical Complications. The secondary aim was to determine the impact of obesity on post-operative outcomes in the subgroup of patients undergoing laparoscopic CRC resection.

MATERIALS AND METHODS

Study design

The Prince Charles Hospital (TPCH) CRC Database includes all patients who have undergone CRC resection at our institution. The criteria for inclusion in TPCH CRC Database were all patients who had histologically confirmed CRC (including appendiceal cancers as per the International Classification of Diseases-10 classification) and underwent an operation at TPCH between January 2010 and December 2020. As

per the WHO definition, patients were grouped into an obese group (BMI ≥ 30) or non-obese group (BMI < 30), and the demographic features, co-morbidities, and surgical features in each group were reported and compared. In addition, the post-operative outcomes of patients in each group were also compared.

Ethics approval

Approval for the TPCCH Colorectal Cancer Database was granted by TPCCH Human Research Ethics Committee (HREC/17/QPCH/295).

Demographics and co-morbidities

Demographic data documented in this study included age, gender, BMI, smoking and alcohol status. Patient co-morbidities were categorised into cardiac, respiratory and metabolic aetiologies, with specific diseases recorded in each category if present. The American Society of Anaesthesiologists (ASA) grade was also recorded (Table 1).

Surgical features

Surgical features recorded included cancer location, operative urgency, operative approach, colorectal operation performed, requirement for stoma, and peri-operative requirement for transfusion (Table 2).

Post-operative outcomes

Post-operative outcomes recorded included the occurrence of any post-operative complication, which were each graded by the Clavien-Dindo Classification of Surgical Complications (Supplementary material). Complications were also classified as either no complication/low-grade and high-grade, defined as Clavien-Dindo grades I-II and III-V respectively. In addition, complications were attributed to either a surgical or medical cause, with specific surgical and medical complications also recorded if they occurred (Table 3).

The outcomes as above were also undertaken in the subgroup of patients undergoing laparoscopic surgery (Table 4). Patients who underwent laparoscopic surgery who were converted to an open procedure intra-operatively were excluded from this subgroup. Furthermore, post-operative outcomes of obese *vs* non-obese patients were compared in subgroups divided by cancer location. Patients were divided into a right sided colon cancer (caecum to transverse colon) subgroup (Table 5), left sided colon cancer (splenic flexure to sigmoid colon) subgroup (Table 6) and a rectal cancer subgroup (Table 7).

Statistical analysis

Statistical analysis was performed using Stata v17 (StataCorp). Categorical variables were presented as frequencies, and continuous variables were presented as medians and interquartile ranges. Groups were assessed using *t*-test, Chi-squared test or Fisher's exact test as appropriate. Statistically significant results were defined at the level of $P \leq 0.05$.

RESULTS

Patient demographics and co-morbidities

From January 2010 to December 2020, six-hundred and fifteen patients at our institution fulfilled the inclusion criteria and were included in the database. One-hundred and eighty-two patients (29.6%) had a BMI of 30 or above (obese group), and four-hundred and thirty-three patients (70.4%) had a BMI below 30 (non-obese group). Table 1 outlines and compares the demographic features and co-morbidities in both groups.

Patients in both groups were of similar age (obese group, 70 years *vs* non-obese group, 71 years, $P = 0.45$) and gender (45.6% male *vs* 53.6% male, $P = 0.08$). In contrast, the obese group had a greater proportion of patients graded at a higher ASA grade (ASA I-II: 29.7% *vs* 45.7%, ASA \geq III: 70.3% *vs* 54.3%, $P < 0.001$), and also had a higher prevalence of cardiac co-morbidities (73.1% *vs* 56.8%, $P < 0.001$) and respiratory co-morbidities (37.4% *vs* 26.8%, $P = 0.01$) compared to patients in the non-obese group.

Obese patients were more likely to have type II diabetes mellitus (28.6% vs 12.7%, $P < 0.001$).

Surgical features

Table 2 outlines and compares the surgical features between the obese and non-obese groups. Both groups had a similar proportion of elective and emergency procedures (88.5% vs 82.9% and 11.5% vs 17.1% respectively, $P = 0.09$). The obese group had a higher proportion of patients requiring conversion to an open procedure (12.8% vs 5.1%, $P = 0.002$). Both groups had a similar percentage of patients requiring peri-operative blood transfusion (15.4% vs 15.0%, $P = 0.90$).

Post-operative outcomes

Table 3 outlines and compares the post-operative outcomes and complications between the obese and non-obese groups. There were no significant differences between groups in terms of the prevalence of post-operative complications (51.6% vs 44.1%, $P = 0.06$) or high-grade complications (19.2% vs 14.1%, $P = 0.11$). In-hospital mortality (Clavien-Dindo V) occurred in 1 obese patient (0.5%) and 8 non-obese patients (1.8%). There were no differences between both groups in the incidence of surgical complications (26.4% vs 22.9%, $P = 0.35$), including, but not limited to, anastomotic leak (3.8% vs 2.8%, $P = 0.46$), wound infection (3.8% vs 4.4%, $P = 0.83$) and return to theatre (3.8% vs 3.0%, $P = 0.62$). The prevalence of post-operative medical complications was also similar between both groups (20.3% vs 22.2%, $P = 0.67$), and there were no differences in the prevalence of specific medical complications. The median post-operative length of stay was also similar between both groups (7 d vs 6 d, $P = 0.42$).

Post-operative outcomes in patients undergoing laparoscopic surgery

Four-hundred and seventy-two patients (76.7%) underwent laparoscopic and laparoscopic-assisted surgery. Three-hundred and thirty-six patients (71.2%) had a BMI below 30, and one-hundred and thirty-six patients (28.8%) had a BMI of 30 or above.

Obese patients in the laparoscopic surgery subgroup similarly had a higher ASA grade (ASA I-II: 36.8% vs 48.1%, ASA \geq III: 63.2% vs 51.9%, $P = 0.03$), and a higher prevalence of pre-existing cardiac co-morbidities (72.8% vs 56.3%, $P < 0.001$) and respiratory co-morbidities (38.2% vs 26.9%, $P = 0.02$) compared to non-obese patients.

Post-operative outcomes of the patients in the cohort undergoing laparoscopic surgery are shown in Table 4. Obese patients were more likely to experience a post-operative complication (47.8% vs 39.3%, $P = 0.05$), however there was no differences between both groups in the incidence of high-grade complications (17.6% vs 11.0%, $P = 0.07$). There were similarly no major differences between both groups in the percentage of patients who experienced a surgical complication (27.2% vs 20.2%, $P = 0.11$) or medical complication (15.4% vs 19.6%, $P = 0.36$). The median post-operative length of stay was equivalent between both groups (6 d vs 6 d, $P = 0.15$).

Post-operative outcomes of obese vs non-obese patients based on cancer location

Obese and non-obese patients in the right sided colon cancer subgroup had equivalent outcomes, with no differences in the incidence of post-operative complications (52.2% vs 54.1%, $P = 0.61$), high-grade complications (17.4% vs 15.6%, $P = 0.73$), surgical complications (23.9% vs 25.4%, $P = 0.88$), or medical complications (27.2% vs 26.8%, $P = 1.00$). Similarly in the left sided colon cancer subgroup there were no differences between obese and non-obese patients in the percentage of post-operative complications (47.5% vs 37.1%, $P = 0.09$), high grade complications (18.0% vs 9.8%, $P = 0.11$), surgical complications (27.9% vs 20.3%, $P = 0.27$), or medical complications (9.8% vs 19.6%, $P = 0.10$). In the rectal cancer subgroup, there were also no differences between obese and non-obese patients in the prevalence of post-operative complications (70.0% vs 54.2%, $P = 0.68$), high-grade complications (35.0% vs 31.2%, $P = 0.78$), surgical complications (35.0% vs 37.5%, $P = 1.00$), or medical complications (25.0% vs 27.1%, $P = 1.00$).

DISCUSSION

We have found that despite patients with an obese BMI having significantly higher rates of cardiac co-morbidities, respiratory co-morbidities, type II diabetes mellitus, and conversion to open surgery compared to patients with a non-obese BMI, there was no increased prevalence of post-operative complications (51.6% vs 44.1%, $P = 0.06$) or high-grade complications (19.2% vs 14.1%, $P = 0.11$) following CRC surgery. Our findings are concordant with Genser *et al*^[12], who reported that in patients undergoing emergency colon cancer surgery, obese patients did not experience a higher proportion of post-operative complications (54% vs 52%, $P = 0.86$) or high-grade complications (20% vs 17%, $P = 0.47$). Despite our obese cohort having a higher burden of medical co-morbidities, we did not observe an increased rate of specific post-operative medical complications. Smith *et al*^[13] has also shown that obese patients are not at an increased risk of post-operative pneumonia or renal failure; and Merkow *et al*^[14], has shown that obese patients are similarly at no increased risk of post-operative pneumonia, as well as cardiac arrest, myocardial infarction or stroke. Obesity may not be an independent predictor for peri-operative cardiac complications, with the latter demonstrated to be more accurately related to functional status rather than traditional cardiovascular risk factors^[15].

Importantly, we have determined that the impact of obesity on post-operative outcomes may only manifest in patients undergoing laparoscopic resection, with obese patients in this subgroup having a significantly increased prevalence of post-operative complications (47.8% vs 39.3%, $P = 0.05$). It should be noted that these findings were not influenced by patients who underwent laparoscopic converted to open surgery given that they were excluded from this subgroup.

In contrast to our findings, a Chinese study by Xia *et al*^[16] reported that following laparoscopic CRC resection, patients BMI of ≥ 30 had a higher but non-significant incidence of Clavien-Dindo grade III complications compared to patients with a BMI of < 25 (14.3% vs 5.1%, $P = 0.178$). Similarly, a Korean study on laparoscopic CRC outcomes by Park *et al*^[17] also showed that obesity was not associated with an increased rate of major post-operative complications including ileus, bleeding and anastomotic

leak (7.4% *vs* 5.3%, $P = 0.889$). Non-significant results in both these studies may be related to the lower prevalence of obesity in Asian countries, which is reflected by both studies having only 2.7% of their cohorts categorised as BMI ≥ 30 . Two systematic reviews of laparoscopic CRC surgery outcomes in the obese by Fung *et al*^[18] and He *et al*^[19] have both reported obesity to be associated with increased overall post-operative morbidity [odds ratio (OR) = 1.54, 95% confidence interval (CI): 1.21-1.97 and OR = 1.40, 95%CI: 1.18-1.66 respectively].

It is widely recognised that visceral obesity is associated with increased intra-operative technical difficulty by reducing access and visualisation from thickened omentum and mesentery, distorting surgical planes, and increasing the risk of bleeding from both difficult mobilisation of vessels and friable fatty tissue^[20]. Our finding of poorer post-operative outcomes in obese patients undergoing laparoscopic surgery and not the obese cohort in general may be due to the fact that these aforementioned issues are aggravated in a laparoscopic approach, where increased intra-abdominal adiposity may severely restrict the already small working space available during a minimally-invasive resection. In addition, obese patients are pre-disposed to having a reduced physiologic reserve, and are thus at a greater risk of haemodynamic compromise during pneumoperitoneum from both increased intra-abdominal pressure and systemic acidosis secondary to carbon dioxide absorption^[21].

In the modern era, laparoscopic surgery has been established as the standard of care in CRC surgery^[22]. Although we have shown utilising this approach is associated with an increased prevalence of general post-operative complications in obese patients, we acknowledge that there are circumstances where the well-recognised benefits of laparoscopic surgery such as earlier restoration of gut motility, reduced post-operative pain and shorter length of stay may outweigh the perceived risks^[23,24]. Martin and Stocchi^[25] has proposed several practical strategies during laparoscopic colectomy in the obese such as the use of a 30-degree laparoscope to facilitate exposure and 10 mm instruments to allow for greater leverage during retraction, as well as the use of intra-corporeal vessel ligation given potential difficulties in exteriorising thickened omentum.

Surgeons attempting a laparoscopic approach in obese patients should be adequately experienced and aware that the benefits of laparoscopic surgery likely diminish if meaningful progress in the operation is not made.

We recognise that as an anthropometric measure, BMI has its limitations in the ability to identify visceral obesity, and also is distributed differently among ethnic groups^[26]. Our rationale for using BMI as opposed to more specific volumetric measures of intra-abdominal adiposity such as visceral fat area, is that BMI is a much more commonly used definition of obesity in the literature. This enabled us to compare our outcomes directly against a larger number of studies. In addition, given that BMI is indicative of whole-body fat, it also allows for the analysis of general adipose-associated pathophysiological processes^[19].

We have found that despite patients with an obese BMI having significantly higher rates of cardiac co-morbidities, respiratory co-morbidities, type II diabetes mellitus, and conversion to open surgery compared to patients with a non-obese BMI, there was no increased prevalence of post-operative complications (51.6% vs 44.1%, $P = 0.06$) or high-grade complications (19.2% vs 14.1%, $P = 0.11$) following CRC surgery.

CONCLUSION

Surgical resection of CRC in obese individuals is safe. A higher prevalence of post-operative complications in obese patients appears to only be in the context of laparoscopic surgery.

ARTICLE HIGHLIGHTS

Research background

Obesity is a worldwide epidemic of increasing significance. Although the colorectal surgeons of today manage a greater number of obese patients with colorectal cancer (CRC), the current literature reports inconsistent findings on whether this phenomenon impacts post-operative outcomes following CRC surgery.

Research motivation

This research was conducted to determine whether obese patients had equivalent outcomes compared to non-obese patients following CRC surgery. This is an important issue, as there is no consensus on whether obesity truly impacts post-operative outcomes, yet obese patients are at risk of having their surgery withheld or delayed based on this factor alone.

Research objectives

The primary aim of this study was to compare the post-operative outcomes of obese vs non-obese patients following CRC surgery. With laparoscopic surgery now recognised as the standard of care in CRC management, post-operative outcomes between obese and non-obese patients were also analysed in the subgroup of patients undergoing laparoscopic CRC surgery.

Research methods

Patients who underwent CRC resection between January 2010 and December 2020 at the Prince Charles Hospital, Queensland, Australia were included in this study. As per the World Health Organization definition, this study defined obesity as a body mass index (BMI) of 30 mg/kg² and above. Patients were divided into an obese and non-obese group, and post-operative outcomes were compared between these two groups using parametric and non-parametric tests. This study also analysed the post-operative outcomes of obese vs non-obese patients in the subgroup undergoing laparoscopic CRC surgery.

Research results

This research has demonstrated that although obese patients were more likely to experience conversion to an open procedure ($P = 0.002$), they did not experience more post-operative complications ($P = 0.06$) or high-grade complications ($P = 0.11$). There were also no differences in in-hospital mortality ($P = 0.06$) or length of stay ($P = 0.42$). In

the laparoscopic subgroup however, patients were more likely to experience a post-operative complication ($P = 0.05$), but did not experience more high-grade complications ($P = 0.07$).

Research conclusions

Our study has determined that obesity is no barrier to adequate post-operative outcomes following CRC surgery, with obese patients having equivalent post-operative outcomes compared to their non-obese counterparts. Caution is advised however, when attempting a laparoscopic approach in obese patients.

Research perspectives

Although BMI is a well-recognised and accepted surrogate marker of obesity, further studies in this area should analyse post-operative outcomes using other markers of visceral obesity. In addition, the effect of nutritional status and body composition on post-operative outcomes can be explored.

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