HHS Public Access

Author manuscript

J Gastrointest Surg. Author manuscript; available in PMC 2017 August 17.

Published in final edited form as:

J Gastrointest Surg. 2017 March ; 21(3): 534–542. doi:10.1007/s11605-017-3362-9.

Quantitative Assessment of Visceral Obesity and Postoperative Colon Cancer Outcomes

Oluwatobi. O. Ozoya[*,1,2], **Erin M. Siegel**[*,1,3], **Thejal Srikumar**[1,4], **Amanda M. Bloomer**[1], **Amanda DeRenzis**[1], and **David Shibata**[5]

[1]Cancer Epidemiology, Moffitt Cancer Center, Tampa FL

[2]Department of Global Health, College of Public Health, University of South Florida, Tampa, FL

[3]Health Research Informatics, Moffitt Cancer Center, Tampa, FL

[4]Morsani College of Medicine, University of South Florida, Tampa, FL

[5]Department of Surgery, UT West Cancer Center, University of Tennessee Health Science Center, Memphis, TN

Abstract

Background—Quantitative computed tomography (CT) assessment of visceral adiposity may be superior to body mass index (BMI) as a predictor of surgical morbidity. We sought to examine the association of CT measures of obesity and BMI with short-term post-operative outcomes in colon cancer patients.

Methods—In this retrospective study, 110 patients treated with colectomy for Stage I–III colon cancer were classified as obese or non-obese by pre-operative CT-based measures of adiposity or BMI. [Obese: BMI≥30kg/m^2, visceral fat area (VFA) to subcutaneous fat area ratio (V/S) ≥0.4 and VFA>100cm^2)]. Post-operative morbidity and mortality rates were compared.

Results—Obese patients, by V/S and VFA but not BMI, were more likely to be male and have pre-existing hypertension and diabetes. The overall complication rate was 25.5% and there were no mortalities. Obese patients by VFA (with a trend for VS but not BMI) were more likely to develop postoperative complications as compared to patients classified as non-obese; VFA (30.5% vs.10.7%, p= 0.03), VS (29.2% vs. 9.5%, p=0.05) and BMI (32.4% vs. 21.9%, p=0.23).

Corresponding Author: David Shibata, MD FACS FASCRS, Scheinberg Endowed Chair of Surgery, Professor and Chair, Department of Surgery & Deputy Center Director, University of Tennessee Health Science Center, 910 Madison Avenue, Room 203, Memphis, TN 38163, Tel 901-448-5914, Fax 901-448-7306, dshibata@uthsc.edu.

*These authors contributed equally to this work.

Author contributions:

Substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data- OO, ES, DS, TS, AB, AD

Drafting the article or revising it critically for important intellectual content- DS, ES, OO, AB, TS, AD

Final approval of the version to be published- DS, ES, OO, AB, TS, AD

Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved- ES, DS, OO, AB, TS, AD

Conclusions—Elevated visceral obesity quantified by CT is associated with the presence of key metabolic comorbidities and increased post-operative morbidity and may be superior to BMI for risk stratification.

Keywords

Computed tomography; visceral obesity; colon cancer; surgical complication

INTRODUCTION

Obesity in the US has reached epidemic proportions with an estimated 66% of the population being classified as overweight and/or obese[1]. Obesity is thought to play a contributing role in the development and prognosis of a number of cancers[2, 3]. In particular, obesity is associated with more than 20% of colon cancer-related deaths in the US[4]. Colorectal cancer remains the second most common cause of yearly cancer-related mortality across gender, with approximately 51,900 annual deaths[5].

The body mass index (BMI) is a conventional tool used to derive body weight categories and for calculating chemotherapy dosage. Nevertheless, the association between BMI as a measure of obesity and adverse surgical outcomes in colorectal cancer remains inconsistent[6, 7]. This may be due to inaccurate estimation of body fat distribution.

Adipose tissue distribution in the body is diverse, but visceral fat compared to subcutaneous fat tissue appears to enhance adverse metabolic outcomes[8, 9]. Besides metabolic syndrome, excess visceral fat is thought to predispose to chronic inflammation and release of growth factors that mediate colonic neoplasia[10, 11]. Conventional methods for estimating intra-abdominal fat include waist circumference and waist-to-hip ratio[12, 13] and BMI, but they do not clearly distinguish subcutaneous fat distribution from visceral fat[6, 14, 15].

More precise distinction of fat distribution may improve prognostication of outcomes of surgery among colon cancer patients. Significant associations have been described between visceral adiposity and rectal cancer treatment outcomes[6, 16]. Recent studies have utilized quantitative computed tomography (CT) to determine visceral obesity by measuring visceral fat area (VFA)[17] or visceral fat/subcutaneous fat area (V/S ratio)[18] and significant associations have been reported. A VFA of >100 cm^2 or V/S > 0.4 is associated with the metabolic syndrome[19] and poor surgical outcomes[6, 17]. Moreover, diagnostic CT adiposity measurements before colon cancer surgery, have yielded a significant association with short term complications such as wound complication, venous thrombosis and incisional hernia, compared to BMI[20, 21].

In the current study, we sought to examine the association between CT measures of visceral adiposity and short-term surgical outcomes in a relatively homogeneous group of Stage I–III colon cancer patients.

MATERIALS AND METHODS

This research is part of a larger prospective cohort of 437 colon and rectal cancer patients evaluating factors associated with short- and long-term patient outcomes. The total population of 437 had more males (58%) compared with females (42%) and both had a mean age of 64 years. The disease distribution in the total population was 53.7% (235) of patients diagnosed with cancer in the colon and rectosigmoid junction, 44.6% (195) rectal cancer and 1.6% (7) had stage 0 disease (*in situ* or no evidence of disease). All patients provided informed consent.

Patient selection and chart review

For this IRB-approved study, a cohort of 110 patients who had surgery for non-metastatic colon cancer performed at the Moffitt Cancer Center between 2006 and 2015 with pre-operative CT images available were identified. Data were abstracted on patient demographics, preoperative comorbidities, TNM stage, histological grade and any complications within 30 days following surgery. Medical records were reviewed by trained clinicians who abstracted data on standardized abstraction forms. Abstracted data were logged into a secure Microsoft Access database.

Short term post-surgery morbidity

The nature of the complications included was either surgical or medical during the first 30 days following resection. Specific morbidities were recorded as documented in medical records. In addition, the Clavien-Dindo comorbidity grading system was utilized to further classify documented outcomes prior to statistical analysis[22]. The Clavien-Dindo scale includes: Grade 1 (deviation from normal postoperative course without the need for pharmacological, surgical endoscopic or radiological interventions), Grade II (requiring pharmacological, blood transfusion and total parenteral nutrition), Grade III (requiring surgical, endoscopic or radiological intervention) and Grade IV (life threatening complications requiring intensive care unit management) and Grade V (death of a patient). Patients who had at least one complication were included and those who had more than one complication were classified using the highest grade of reported complication[22, 23].

Adiposity measurement

Patients included in the study had availability of an archived preoperative digitized CT scan (n = 110). Radiologic measurement was performed on diagnostic CT scans using a GE AW digital workstation (General Electric Healthcare). As previously reported[16], adipose tissue was segmented by setting the CT attenuation level between −190 and −30 Hounsfield units with subsequent delineation of visceral and subcutaneous regions. Visceral and subcutaneous fat areas were quantified using CT axial slices taken at the L4–L5 intervertebral span[16, 24, 25]. The VFA to SFA ratio (V/S) was computed as a parameter for visceral adiposity as previously described.[16] The threshold for elevated V/S was set at 0.4[16, 26, 27] while visceral fat area (VFA) greater than 100 cm^2 was selected[2, 15, 17, 18]. The error rate was set at 0.5% as previously described[25, 27]. BMI was calculated for each subject from the height and weight in standard fashion.

Statistical analysis

BMI and V/S-determined adiposity were analyzed as continuous measures or categorized using a pre-determined cut point (BMI ≥ 30 kg/m^2, V/S ≥ 0.4 and VFA≥100 cm^2). As appropriate, chi-square or Fischer's exact tests (categorical) or 2 sample t-test with equal or unequal variance (continuous), were used to determine differences in adiposity based on clinical, pathological and perioperative features. The Clavien-Dindo scale was merged into two groups; Minor- grade I and II and Major- grade III and IV. All statistical tests were 2-sided and deemed statistically significant at the level of 0.05 unless otherwise specified. Analyses were performed using SPSS (IBM SPSS Statistics 22).

RESULTS

Demographics and clinical features

The study population consisted of 110 patients with non-metastatic colon cancer (Stage I – III) and a mean age of 66 years ± 12 years (Table 1). There were slightly more male patients than females (n = 60 versus n = 50), and almost all patients were white (94%). The frequencies of hypertension, diabetes, and hypercholesterolemia were 50.9%, 11.8% and 31.8% respectively.

The majority of cases were performed laparoscopically (66%) while open (33%) and hybrid (1%) accounted for other approaches. Thirty-four percent of patients had a BMI ≥ 30 kg/m^2, while 81% of patients were classified as obese by V/S (≥ 0.4) and 75% by VFA(> 100 cm^2).

Body mass index and visceral obesity by sex

A complete description of BMI and visceral adiposity variables stratified by gender is presented in Table 2. Overall mean BMI of these colon cancer patients was 28.2 ± 5.8 kg/m^2 and the mean BMI for male gender was not significantly different from female (28.8 ± 5.2 vs 27.5 ± 6.4 kg/m^2, $p = 0.24$). In contrast, mean visceral obesity among males was significantly higher than that in females (males vs females for VS: 0.81 ± 0.43 vs 0.50 ± 0.2, p < 0.001 and VFA: 191.5 ± 93 vs 142 ± 81.4cm^2, p=0.004).

Adiposity measures by preoperative characteristics

A summary of selected preoperative variables as a function of BMI, V/S and VFA is presented in Table 3. With respect to mean BMI, colon cancer patients with hypertension, diabetes and hypercholesterolemia did not differ from those without these conditions (p = 0.15; $p = 0.67$; $p = 0.74$ respectively). Pathological stage, complications or grade of complication were not associated with significant differences in mean BMI ($p = 0.40$; p= 0.16; $p = 0.37$). In contrast to BMI, colon cancer patients with V/S ≥ 0.4 were significantly more likely to be male (61.8% vs 23.8%; $p = 0.002$) and have pre-existing hypertension (56.2% vs 28.6%, $p = 0.02$) compared to those with V/S < 0.4. Patients with V/S ≥ 0.4 had marginally significant likelihood of having pre-existing diabetes. Similar finding were observed when V/S was considered as a continuous measure with mean V/S ratio significantly higher in patients with pre-existing hypertension (0.76 ± 0.39 vs 0.57 ± 0.37; p = 0.01) and diabetes (0.95 ± 0.51 vs 0.63 ± 0.35; $p = 0.004$) compared to patients who did not have those pre-existing conditions. When visceral obesity was defined by VFA alone,

colon cancer patients with VFA≥100 cm^2 were significantly more likely to be males (61% vs 39%; $p = 0.02$) and have pre-existing hypertension (63% vs 37%; $p < 0.001$) diabetes (16% vs 84%; $p = 0.04$) compared to those with VFA<100 cm^2. Similar results were observed when VFA was evaluated as a continuous variable.

Adiposity measures by postoperative outcomes

The overall complication rate was 25.5% (28/110) with no mortality (Supplemental Table). Short term complications included wound infection (8), seroma (5), anastomotic leaks (4), arrhythmia (3), ileus/small bowel obstruction (2), thromboembolism (2), wound hematoma (2), wound dehiscence (1) and urinary retention (1). The association between postoperative variables and adiposity measures are presented in Table 4. In contrast to BMI, patients who developed postoperative complications had statistically significant higher mean V/S and VFA than those who did not develop complications (0.40 cm^2 vs 0.36 cm^2, $p = 0.003$; 213 ± 92 cm^2 vs 154 cm^2, $p = 0.003$). Obese patients by VFA (with a trend for VS but not BMI) were more likely to develop post-op complications as compared to patients who were classified as non-obese; VFA (30.5% vs 10.7%, p =0.03), VS (29.2% vs. 9.5%, p =0.05), and BMI (32.4% vs 21.9%, p =0.23). The severity of postoperative complications as classified by the Clavien-Dindo grading method was not significantly associated with obesity categorized by BMI, V/S and VFA ($p = 0.37$; $p = 0.80$; $p = 0.11$).

DISCUSSION

The impact of BMI on surgical outcomes in colon cancer patients has remained somewhat controversial. This uncertainty may be related to the fact that BMI does not take into account the distribution of body fat. In the current study, BMI was not associated with key co-morbid factors and was not predictive of post-operative morbidity. However, we observed a negative association between radiologically-determined visceral obesity (V/S and VFA) and key pre-operative metabolic comorbidities in colon cancer patients. Compared to BMI, CT-classified visceral obesity was associated with short-term complications; however there was no association with the severity of complications as defined by the Clavien-Dindo grading method.

The observed association between visceral obesity and preoperative metabolic comorbidities is consistent with previous studies that have linked cardiovascular risk factors to increased visceral fat[19]. Hiuge-Shimizu et al. have reported that VFA and SFA were associated with obesity-related diabetes and hypertension whereas BMI was not[18, 19]. In addition, VFA ≥ 100cm^2 has been shown to be associated with obesity-related cardiovascular risk factors[25] and increased odds of developing coronary artery disease[28]. Males were more likely to be viscerally obese than women in our study. This finding supports work by Cakir et al. which showed that males were more represented in the viscerally obese class as compared to non-obese[15]. In contrast, our study found no difference in obesity by gender when BMI was used. These particular observations are similar to those reported by Healy et a. in which they noted no significant differences in major morbidity using BMI-classified obesity[29]. Our findings suggest that radiologic measures of visceral obesity may be superior to BMI in gender-based preoperative risk stratification.

Herein, our study suggests that visceral obesity as defined by V/S and VFA is significantly associated with a higher rate of postoperative complications. This finding is supported by Watanabe et al., who showed that among a cohort of colon cancer patients, visceral obesity is superior to BMI in predicting short term post-operative morbidity in colon cancer patients[17]. Our study did not yield any association between BMI and complication rate. Makino et al. reported similar findings where short term complication rates did not differ between 76 obese and non-obese colon cancer surgery patients using BMI[30]. Regardless of pre-existing co-morbidities, visceral obesity remains a significant independent risk factor for complications following colon cancer surgery[31].

The precise biological mechanisms that underlie the association between obesity and colon cancer surgery outcomes remain under investigation. A number of factors such as impaired inflammatory response, microvascular dysfunction[32, 33], poor tissue oxygen tension (skin, wound, and adipose)[34] are implicated. Despite antibiotic prophylaxis, subtherapeutic tissue antibiotic concentrations are observed in obese patients and may facilitate wound infection.[35, 36]. In addition, the development of wound infection may be enhanced by an attenuated inflammatory response secondary to endotoxin tolerance in obese patients[37, 38]. A stronger understanding of the contribution of obesity to surgical site infection would be valuable given its association with subsequent risk of systemic infection and worse long-term outcomes.[3]. Seroma formation in colon cancer surgery is less studied compared to breast surgery but has been linked to obesity, wound dead space, technique and comorbidity among other factors[39, 40]. In addition, seroma has been linked with increased risk of postoperative wound infection, hematoma formation, cancer recurrence and poor long-term survival[41, 42]. Anastomotic leaks have been associated with risk factors such as smoking, distal rectal cancers and obesity (BMI > 25kg/m^2)[43, 39].

The observed poor outcomes among viscerally obese patients may in part, be attributable to the technical challenges arising from excess intraabdominal fat encountered during operation[16, 23]. Of note, in this study, surgical approach (open vs. laparoscopic) was not a predictor of increased complications among visceral obesity groups whether categorized by BMI, V/S or VFA as compared to non-obese counterparts (Supplemental Table 2). Moreover, the proportion of laparoscopic cases was fairly equal between obese and non-obese groups across BMI, VS and VFA. (Supplemental Table 2). As such, differences in rates of post-operative morbidity are not explained by surgical approach.

The incidence of atrial fibrillation following colon cancer surgery hast not been well studied however, obesity and the metabolic syndrome has been linked with new onset arrhythmia (atrial fibrillation)[44, 45]. Proposed mechanisms for the onset of atrial fibrillation in the setting of metabolic syndrome include electro-mechanical remodeling of the left atrium from induced renin-angiotensin-system (RAAS), hemodynamic and autonomic dysfunction[44, 45]. The obesity-cancer transformation relationship is still under investigation but proposed mechanisms include lipotoxicity, chronic inflammation, metabolic dysfunction, adipose distribution (not mass) and hormonal dysregulation[27, 46–49].

A limitation of this study is its observational nature and inherent accompanying biases. CT measurement of visceral fat is operator-dependent and more time consuming than BMI

measurement, yet the findings of this study suggest that CT measurements may be a useful complement to BMI in quantifying obesity among colon cancer patients. The relatively small sample size restricted analytic power and complication types could not be individually examined for significance. It could also be argued that our findings may not be generalizable as the study population represents a non-metastatic colon cancer sample of predominantly white patients from a single center. Conducting similar studies among different racial and ethnic groups are indicated to further validate our observations. Nonetheless, our sample population was fairly homogeneous with restriction to stage I to III (non-metastatic) colon cancer patients. This further reduced variances in outcomes that may have been due to the stage or treatment and removed the influence of the impact of metastatic disease and/or cachexia on body fat composition. We also ensured that CT measurement was performed on pre-treatment scans closest to surgery to ensure a more accurate reflection of visceral adipose tissue at time of surgery.

Notably, our observation that visceral obesity (rather than BMI) was associated with pre-existing metabolic abnormalities provide further evidence for its biological relevance. Although our study has focused on short term outcomes, further examination of the impact of visceral adiposity status on long term outcomes are warranted. It is conceivable that accurately quantified visceral obesity may serve as a predictor of both short- and long-term outcomes in patients with non-metastatic colon cancer.

CONCLUSION

The obesity epidemic in this country may have a significant impact on surgical outcomes among colon cancer patients. The traditionally-used measure of BMI may be limited by its lack of quantification of visceral fat distribution. We have demonstrated that excess CT-measured visceral adiposity is associated with the presence of key metabolic co-morbidities and an increased rate of short-term post-operative complications following colon cancer resection. Larger studies are warranted to further determine the role of radiologic visceral fat assessment for pre-operative risk stratification in colon cancer patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank Jaime Corvin, Ph.D and Nnadozie Emechebe, BPharm, MPH for reviewing certain aspects of the study.

Grant Support: This work was supported in part by the Moffitt Cancer Center TJS Colorectal Cancer Research Fund and the Bankhead Coley New Investigator Grant (09BN-13).

References

1. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. Jama. 2014; 311(8):806–14. DOI: 10.1001/jama.2014.732 [PubMed: 24570244]

2. Cowey S, Hardy RW. The metabolic syndrome: A high-risk state for cancer? The American journal of pathology. 2006; 169(5):1505–22. DOI: 10.2353/ajpath.2006.051090 [PubMed: 17071576]
3. Gendall KA, Raniga S, Kennedy R, Frizelle FA. The impact of obesity on outcome after major colorectal surgery. Diseases of the colon and rectum. 2007; 50(12):2223–37. DOI: 10.1007/s10350-007-9051-0 [PubMed: 17899278]
4. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. The New England journal of medicine. 2003; 348(17):1625–38. DOI: 10.1056/NEJMoa021423 [PubMed: 12711737]
5. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA: a cancer journal for clinicians. 2013; 63(1):11–30. DOI: 10.3322/caac.21166 [PubMed: 23335087]
6. Cakir H, Heus C, van der Ploeg TJ, Houdijk AP. Visceral obesity determined by CT scan and outcomes after colorectal surgery; a systematic review and meta-analysis. International journal of colorectal disease. 2015; 30(7):875–82. DOI: 10.1007/s00384-015-2174-1 [PubMed: 25772271]
7. Gradmark AM, Rydh A, Renstrom F, De Lucia-Rolfe E, Sleigh A, Nordstrom P, et al. Computed tomography-based validation of abdominal adiposity measurements from ultrasonography, dual-energy X-ray absorptiometry and anthropometry. The British journal of nutrition. 2010; 104(4):582–8. DOI: 10.1017/s0007114510000796 [PubMed: 20370942]
8. Carr DB, Utzschneider KM, Hull RL, Kodama K, Retzlaff BM, Brunzell JD, et al. Intra-abdominal fat is a major determinant of the National Cholesterol Education Program Adult Treatment Panel III criteria for the metabolic syndrome. Diabetes. 2004; 53(8):2087–94. [PubMed: 15277390]
9. Nakao YM, Miyawaki T, Yasuno S, Nakao K, Tanaka S, Ida M, et al. Intra-abdominal fat area is a predictor for new onset of individual components of metabolic syndrome: MEtabolic syndRome and abdominaL ObesiTy (MERLOT study). Proceedings of the Japan Academy Series B, Physical and biological sciences. 2012; 88(8):454–61.
10. Vucenik I, Stains JP. Obesity and cancer risk: evidence, mechanisms, and recommendations. Annals of the New York Academy of Sciences. 2012; 1271:37–43. DOI: 10.1111/j.1749-6632.2012.06750.x [PubMed: 23050962]
11. Kishida K, Funahashi T, Shimomura I. Adiponectin as a routine clinical biomarker. Best practice & research Clinical endocrinology & metabolism. 2014; 28(1):119–30. DOI: 10.1016/j.beem.2013.08.006 [PubMed: 24417951]
12. Wang Y, Jacobs EJ, Patel AV, Rodriguez C, McCullough ML, Thun MJ, et al. A prospective study of waist circumference and body mass index in relation to colorectal cancer incidence. Cancer causes & control: CCC. 2008; 19(7):783–92. DOI: 10.1007/s10552-008-9141-x [PubMed: 18322811]
13. Nazare JA, Smith J, Borel AL, Aschner P, Barter P, Van Gaal L, et al. Usefulness of measuring both body mass index and waist circumference for the estimation of visceral adiposity and related cardiometabolic risk profile (from the INSPIRE ME IAA study). The American journal of cardiology. 2015; 115(3):307–15. DOI: 10.1016/j.amjcard.2014.10.039 [PubMed: 25499404]
14. Rickles AS, Iannuzzi JC, Mironov O, Deeb AP, Sharma A, Fleming FJ, et al. Visceral obesity and colorectal cancer: are we missing the boat with BMI? Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract. 2013; 17(1):133–43. discussion p.43. DOI: 10.1007/s11605-012-2045-9 [PubMed: 23090279]
15. Cakir H, Heus C, Verduin WM, Lak A, Doodeman HJ, Bemelman WA, et al. Visceral obesity, body mass index and risk of complications after colon cancer resection: A retrospective cohort study. Surgery. 2015; 157(5):909–15. DOI: 10.1016/j.surg.2014.12.012 [PubMed: 25708142]
16. Clark W, Siegel EM, Chen YA, Zhao X, Parsons CM, Hernandez JM, et al. Quantitative measures of visceral adiposity and body mass index in predicting rectal cancer outcomes after neoadjuvant chemoradiation. Journal of the American College of Surgeons. 2013; 216(6):1070–81. DOI: 10.1016/j.jamcollsurg.2013.01.007 [PubMed: 23523147]
17. Watanabe J, Tatsumi K, Ota M, Suwa Y, Suzuki S, Watanabe A, et al. The impact of visceral obesity on surgical outcomes of laparoscopic surgery for colon cancer. International journal of colorectal disease. 2014; 29(3):343–51. DOI: 10.1007/s00384-013-1803-9 [PubMed: 24297037]
18. Hiuge-Shimizu A, Kishida K, Funahashi T, Ishizaka Y, Oka R, Okada M, et al. Absolute value of visceral fat area measured on computed tomography scans and obesity-related cardiovascular risk

factors in large-scale Japanese general population (the VACATION-J study). Annals of medicine. 2012; 44(1):82–92. DOI: 10.3109/07853890.2010.526138 [PubMed: 20964583]

19. Hiuge-Shimizu A, Kishida K, Funahashi T, Ishizaka Y, Oka R, Okada M, et al. Reduction of visceral fat correlates with the decrease in the number of obesity-related cardiovascular risk factors in Japanese with Abdominal Obesity (VACATION-J Study). Journal of atherosclerosis and thrombosis. 2012; 19(11):1006–18. [PubMed: 22785136]
20. Aquina CT, Rickles AS, Probst CP, Kelly KN, Deeb AP, Monson JR, et al. Visceral obesity, not elevated BMI, is strongly associated with incisional hernia after colorectal surgery. Diseases of the colon and rectum. 2015; 58(2):220–7. DOI: 10.1097/dcr.0000000000000261 [PubMed: 25585081]
21. Cecchini S, Cavazzini E, Marchesi F, Sarli L, Roncoroni L. Computed tomography volumetric fat parameters versus body mass index for predicting short-term outcomes of colon surgery. World journal of surgery. 2011; 35(2):415–23. DOI: 10.1007/s00268-010-0888-3 [PubMed: 21153815]
22. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Annals of surgery. 2004; 240(2): 205–13. [PubMed: 15273542]
23. Luglio G, De Palma GD, Tarquini R, Giglio MC, Sollazzo V, Esposito E, et al. Laparoscopic colorectal surgery in learning curve: Role of implementation of a standardized technique and recovery protocol. A cohort study. Annals of medicine and surgery (2012). 2015; 4(2):89–94. DOI: 10.1016/j.amsu.2015.03.003 [PubMed: 25859386]
24. Kvist H, Chowdhury B, Grangard U, Tylen U, Sjostrom L. Total and visceral adipose-tissue volumes derived from measurements with computed tomography in adult men and women: predictive equations. The American journal of clinical nutrition. 1988; 48(6):1351–61. [PubMed: 3202084]
25. Balentine CJ, Marshall C, Robinson C, Wilks J, Anaya D, Albo D, et al. Validating quantitative obesity measurements in colorectal cancer patients. The Journal of surgical research. 2010; 164(1): 18–22. DOI: 10.1016/j.jss.2010.05.048 [PubMed: 20828744]
26. Matsuzawa Y, Nakamura T, Shimomura I, Kotani K. Visceral fat accumulation and cardiovascular disease. Obesity research. 1995; 3(Suppl 5):645s–7s. [PubMed: 8653544]
27. Wajchenberg BL. Subcutaneous and visceral adipose tissue: their relation to the metabolic syndrome. Endocrine reviews. 2000; 21(6):697–738. DOI: 10.1210/edrv.21.6.0415 [PubMed: 11133069]
28. Kishida K, Funahashi T, Matsuzawa Y, Shimomura I. Visceral obesity and cardiometabolic risks: lessons from the VACTION-J study. Clinical Lipidology. 2012; 7(5):579–86.
29. Healy LA, Ryan AM, Sutton E, Younger K, Mehigan B, Stephens R, et al. Impact of obesity on surgical and oncological outcomes in the management of colorectal cancer. International journal of colorectal disease. 2010; 25(11):1293–9. DOI: 10.1007/s00384-010-0963-0 [PubMed: 20563875]
30. Makino T, Trencheva K, Shukla PJ, Rubino F, Zhuo C, Pavoor RS, et al. The influence of obesity on short- and long-term outcomes after laparoscopic surgery for colon cancer: a case-matched study of 152 patients. Surgery. 2014; 156(3):661–8. DOI: 10.1016/j.surg.2014.03.023 [PubMed: 24947645]
31. Esemuede IO, Murray AC, Lee-Kong SA, Feingold DL, Kiran RP. Obesity, regardless of comorbidity, influences outcomes after colorectal surgery-time to rethink the pay-for-performance metrics? Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract. 2014; 18(12):2163–8. DOI: 10.1007/s11605-014-2672-4 [PubMed: 25331964]
32. Singer G, Granger DN. Inflammatory responses underlying the microvascular dysfunction associated with obesity and insulin resistance. Microcirculation (New York, NY: 1994). 2007; 14(4–5):375–87. DOI: 10.1080/10739680701283158
33. Sola E, Vaya A, Espana F, Castello R, Ramon LA, Hernandez-Mijares A, et al. Plasminogen activator inhibitor-1 levels in severe and morbid obesity. Effect of weight loss and influence of 4G/5G polymorphism. Thrombosis research. 2008; 122(3):320–7. DOI: 10.1016/j.thromres. 2007.10.016 [PubMed: 18037477]
34. Fleischmann E, Kugener A, Kabon B, Kimberger O, Herbst F, Kurz A. Laparoscopic surgery impairs tissue oxygen tension more than open surgery. The British journal of surgery. 2007; 94(3): 362–8. DOI: 10.1002/bjs.5569 [PubMed: 17143850]

35. Isla A, Troconiz IF, de Tejada IL, Vazquez S, Canut A, Lopez JM, et al. Population pharmacokinetics of prophylactic cefoxitin in patients undergoing colorectal surgery. European journal of clinical pharmacology. 2012; 68(5):735–45. DOI: 10.1007/s00228-011-1206-1 [PubMed: 22246211]

36. Toma O, Suntrup P, Stefanescu A, London A, Mutch M, Kharasch E. Pharmacokinetics and tissue penetration of cefoxitin in obesity: implications for risk of surgical site infection. Anesthesia and analgesia. 2011; 113(4):730–7. DOI: 10.1213/ANE.0b013e31821fff74 [PubMed: 21642605]

37. Lopez-Collazo E, del Fresno C. Pathophysiology of endotoxin tolerance: mechanisms and clinical consequences. Critical care (London, England). 2013; 17(6):242.doi: 10.1186/cc13110

38. Pena OM, Pistolic J, Raj D, Fjell CD, Hancock RE. Endotoxin tolerance represents a distinctive state of alternative polarization (M2) in human mononuclear cells. Journal of immunology (Baltimore, Md: 1950). 2011; 186(12):7243–54. DOI: 10.4049/jimmunol.1001952

39. Sands GA, Maloney J. Seromas: The Ins and Outs. Journal of Radiology Nursing. 2014; 33(3): 116–20.

40. Srivastava V, Basu S, Shukla VK. Seroma formation after breast cancer surgery: what we have learned in the last two decades. Journal of breast cancer. 2012; 15(4):373–80. DOI: 10.4048/jbc.2012.15.4.373 [PubMed: 23346164]

41. Mukesh MB, Barnett G, Cumming J, Wilkinson JS, Moody AM, Wilson C, et al. Association of breast tumour bed seroma with post-operative complications and late normal tissue toxicity: results from the Cambridge Breast IMRT trial. European journal of surgical oncology: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology. 2012; 38(10):918–24. DOI: 10.1016/j.ejso.2012.05.008

42. Valeta-Magara A, Hatami R, Axelrod D, Roses DF, Guth A, Formenti SC, et al. Pro-oncogenic cytokines and growth factors are differentially expressed in the post-surgical wound fluid from malignant compared to benign breast lesions. SpringerPlus. 2015; 4:483.doi: 10.1186/s40064-015-1260-8 [PubMed: 26361584]

43. Buchs NC, Gervaz P, Secic M, Bucher P, Mugnier-Konrad B, Morel P. Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. International journal of colorectal disease. 2008; 23(3):265–70. DOI: 10.1007/s00384-007-0399-3 [PubMed: 18034250]

44. Asghar O, Alam U, Hayat SA, Aghamohammadzadeh R, Heagerty AM, Malik RA. Obesity, diabetes and atrial fibrillation; epidemiology, mechanisms and interventions. Current cardiology reviews. 2012; 8(4):253–64. [PubMed: 22920475]

45. Watanabe H, Tanabe N, Watanabe T, Darbar D, Roden DM, Sasaki S, et al. Metabolic syndrome and risk of development of atrial fibrillation: the Niigata preventive medicine study. Circulation. 2008; 117(10):1255–60. DOI: 10.1161/circulationaha.107.744466 [PubMed: 18285562]

46. Matafome P, Santos-Silva D, Sena CM, Seica R. Common mechanisms of dysfunctional adipose tissue and obesity-related cancers. Diabetes/metabolism research and reviews. 2013; 29(4):285–95. DOI: 10.1002/dmrr.2395 [PubMed: 23390053]

47. Kasdagly, M., Radhakrishnan, S., Reddivari, L., Veeramachaneni, DN., Vanamala, J. Nutrition. Vol. 30. Burbank; Los Angeles County, Calif: 2014. Colon carcinogenesis: influence of Western diet-induced obesity and targeting stem cells using dietary bioactive compounds; p. 1242-56.

48. Riondino S, Roselli M, Palmirotta R, Della-Morte D, Ferroni P, Guadagni F. Obesity and colorectal cancer: role of adipokines in tumor initiation and progression. World journal of gastroenterology. 2014; 20(18):5177–90. DOI: 10.3748/wjg.v20.i18.5177 [PubMed: 24833848]

49. Iyengar NM, Hudis CA, Dannenberg AJ. Obesity and cancer: local and systemic mechanisms. Annual review of medicine. 2015; 66:297–309. DOI: 10.1146/annurev-med-050913-022228

Table 1

Treated at the Moffitt Cancer Center (n= 110)

	n	%
Age, y, mean ± SD	65.7 ± 11.9	
Gender		
Male	60	54.5
Female	50	45.5
Race		
White	103	93.6
Non-White	4	3.6
Other/Unknown	3	2.7
Comorbid conditions (yes)		
Diabetes	13	11.8
Hypertension	56	50.9
Hypercholesterolemia	35	31.8
Pathologic stage (overall)		
Stage I	31	28.2
Stage II	39	35.4
Stage III	40	36.4
Pathologic T-stage		
T1	19	17.3
T2	19	17.3
T3	42	38.2
T4	30	27.3
Pathologic N-stage		
N0	72	65.5
N1	27	24.5
N2	11	10.0
Histologic Grade		
Well to moderate	98	89.1
Poorly to undifferentiated	12	10.9
Resection margins		
Positive Proximal Margin	0	0.0
Positive Distal Margin	2	1.8
Type of Surgery		
Laparoscopic	73	66.4
Open	36	32.7
Hybrid	1	0.9
Any postoperative complication		
No	82	74.5
Yes	28	25.5
Clavien classification of complications		

	n	%
Grade I	11	10.0
Grade II	12	10.9
Grade III	2	1.8
Grade IV	3	2.7

Table 2

Descriptive Statistics of Adiposity Variables among Colon Cancer patients

	Mean	SD	Median	Minimum	Maximum
Overall					
Weight (kg)	81.3	20.1	79.9	39.8	132.0
Height (cm)	169.0	9.8	168.6	142.8	191.8
BMI	28.2	5.8	27.2	15.0	46.0
VFA	169.1	90.9	162.8	15.8	445.4
SFA	274.0	131.1	242.6	19.3	765.2
VS	0.7	0.4	0.6	0.1	2.0
Females (n = 50)					
Weight (kg)‡	75.4	20.5	73.95	39.8	132.0
Height (cm)‡	165.2	9.4	165.1	142.8	188.0
BMI	27.5	6.4	26.6	15.0	46.0
VFA‡	142.2	81.4	139.3	18.3	363.6
SFA*	302.6	152.9	261.8	19.3	765.2
V/S‡	0.5	0.2	0.4	0.1	1.1
Males (n = 60)					
Weight (kg)	86.1	18.6	84.4	47.4	130.5
Height (cm)	172.2	9.0	172.6	149.5	191.8
BMI	28.8	5.2	28.0	18.9	41.0
VFA	191.5	92.9	185.3	15.8	445.4
SFA	250.3	105.3	225.5	33.6	567.8
V/S	0.8	0.4	0.8	0.2	2.0

*One-way ANOVA testing for mean differences in adiposity variables by sex; $p < 0.05$.

‡One-way ANOVA testing for mean differences in adiposity variables by sex; $p < 0.01$.

Table 3

Characterization of the Relationship between Clinicopathologic Factors and Adiposity Variables

	BMI						VS ratio						VFA					
				< 30	≥ 30					< 0.4	≥ 0.4					< 100	≥ 100	
	Mean	SD	p value	(n =73) N (%)	(n =37) N (%)	p value	Mean	SD	p value	(n = 21) N (%)	(n = 89) N (%)	p value	Mean	SD	p-value	(n = 28) N (%)	(n = 82) N (%)	p-value
Age, mean (SD)				65.1 (12.9)	66.8 (9.8)	0.471				65.1 (13.2)	65.8 (11.7)	0.797				64.0 (14.5)	66.2 (10.9)	0.387
Sex																		
Male	28.79	5.18	0.238	38 (52.1)	22 (59.5)	0.461	0.81	0.43	**<0.001** ǂ	5 (23.8)	55 (61.8)	**0.002** ǂ	191.51	92.94	**0.004** ǂ	10 (35.7)	50 (61.0)	**0.020** *
Female	27.48	6.43		35 (47.9)	15 (40.5)		0.50	0.25		16 (76.2)	34 (38.2)		142.25	81.38		18 (64.3)	32 (39.0)	
Comorbidities																		
Hypertension	28.99	5.56	0.145	36 (49.3)	20 (54.1)	0.639	0.76	0.39	**0.011** *	6 (28.6)	50 (56.2)	**0.023** *	207.50	83.94	**<0.001** ǂ	4 (14.3)	52 (63.4)	**<0.001** ǂ
No Hypertension	27.38	5.97		37 (50.7)	17 (45.9)		0.57	0.37		15 (71.4)	39 (43.8)		129.31	80.65		24 (85.7)	30 (36.6)	
Diabetes	28.84	4.88	0.673	8 (11.0)	5 (13.5)	0.758	0.95	0.51	**0.004** ǂ	0 (0.0)	13 (14.6)	0.070	219.94	94.61	**0.031** *	0 (0.0)	13 (15.9)	**0.036** *
No Diabetes	28.11	5.92		65 (89.0)	32 (86.5)		0.63	.35		21 (100.0)	76 (85.4)		162.31	88.68		28 (100.0)	69 (84.1)	
Hypercholesterolemia	28.47	5.21	0.739	23 (31.5)	12 (32.4)	0.922	0.73	0.43	0.273	4 (19.0)	31 (34.8)	0.200	185.13	85.89	0.208	6 (21.4)	29 (35.4)	0.172
No Hyperchol.	28.07	6.08		50 (68.5)	25 (67.6)		0.64	0.37		17 (81.0)	58 (65.2)		161.65	92.74		22 (78.6)	53 (64.6)	
Pathologic stage																		
Stage I	28.30	6.16	0.404	20 (27.4)	11 (29.7)	0.474	0.76	0.49	0.079	6 (28.6)	25 (28.1)	0.280	185.69	99.75	0.080	7 (25.0)	24 (29.3)	0.296
Stage II	27.25	4.85		28 (38.4)	10 (27.0)		0.56	0.27		10 (47.6)	28 (31.5)		142.51	77.89		13 (46.4)	25 (30.5)	
Stage III	29.01	6.31		25 (34.2)	16 (43.2)		0.71	0.38		5 (23.8)	36 (40.4)		181.25	91.65		8 (28.6)	33 (40.2)	
Grade																		
Well to Moderate	28.18	5.92	0.923	65 (89.0)	33 (89.2)	0.981	0.67	0.40	0.956	19 (90.5)	79 (88.8)	1.000	166.69	90.79	0.426	26 (92.9)	72 (87.8)	0.727
Poorly to Undifferentiated	28.35	4.85		8 (11.0)	4 (10.8)		0.68	0.32		2 (9.5)	10 (11.2)		188.93	93.21		2 (7.1)	10 (12.2)	

*Represents a significance of $p < 0.05$;

ǂRepresents a significance of $p < 0.01$.

Differences in adiposity by clinicopathologic factors determined by one-way ANOVA or Chi-square Fisher's exact test as appropriate.

BMI, body mass index; VFA, visceral fat area; SFA, Subcutaneous fat area; V/S, Visceral fat to subcutaneous fat ratio

Table 4

Characterization of the Relationship between Short-term Outcomes and Adiposity Variables

	BMI						V/S ratio						VFA					
				< 30	≥ 30					< 0.4	≥ 0.4					< 100	≥ 100	
	Mean	SD	p value	(n =73) N (%)	(n =37) N (%)	p value	Mean	SD	p value	(n = 21) N (%)	(n = 89) N (%)	p value	Mean	SD	p-value	(n = 28) N (%)	(n = 82) N (%)	p-value
Type of Surgery																		
Hybrid	32.00		0.254	0 (0)	1 (2.7)	0.330	0.90		0.428	0 (0.0)	1 (1.1)	0.252	269.94		0.346	0 (0.0)	1 (1.2)	0.602
Laparoscopic	27.57	5.37		50 (68.5)	23 (62.2)		0.70	0.42		11 (52.4)	62 (69.7)		173.99	91.47		17 (60.7)	56 (68.3)	
Open	29.37	6.53		23 (31.5)	13 (35.1)		0.61	0.30		10 (47.6)	26 (29.2)		156.44	89.49		11 (39.3)	25 (30.5)	
Postoperative complications																		
No	27.74	5.79	0.156	57 (78.1)	25 (67.6)	0.232	0.61	0.36	**0.003** ≠	19 (90.5)	63 (70.8)	0.093	154.22	85.96	**0.003** ≠	25 (89.3)	57 (69.5)	**0.045** *
Yes	29.54	5.71		16 (21.9)	12 (32.4)		0.86	0.40		2 (9.5)	26 (29.2)		212.75	92.36		3 (10.7)	25 (30.5)	
Complication Grade																		
Grade I	29.69	5.14	0.371	5 (31.3)	6 (50.0)	0.405	0.81	0.44	0.802	1 (50.0)	10 (38.5)	0.925	246.58	94.88	0.105	1(33.3)	10 (40.0)	0.584
Grade II	30.00	5.68		7 (43.8)	5 (41.7)		0.93	0.42		1 (50.0)	11 (42.3)		204.73	84.43		1 (33.3)	11 (44.0)	
Grade III	33.40	10.75		1 (6.3)	1 (8.3)		0.95	0.21		0 (0.0)	2 (7.7)		239.66	59.34		0 (0)	2 (8.0)	
Grade IV	24.60	4.42		3 (18.8)	0 (0.0)		0.70	0.26		0 (0.0)	3 (11.5)		102.84	60.57		1 (33.3)	2 (8.0)	
Merged Clavien Classification																		
Minor	29.85	5.31	0.549	12 (75.0)	11 (91.7)	0.355	0.87	0.43	0.731	2 (100.0)	21 (80.8)	1.000	224.74	90.07	0.144	2 (66.7)	21 (84.0)	0.459
Major	28.12	7.87		4 (25.0)	1 (8.3)		0.80	0.26		0 (0.0)	5 (19.2)		157.57	91.28		1 (33.3)	4 (16.0)	

*Represents a significance of $p < 0.05$;

≠Represents a significance of $p < 0.01$.

Differences in adiposity by short-term outcomes determined by one-way ANOVA or Chi-square Fisher's exact test as appropriate.

BMI, body mass index; VFA, visceral fat area; SFA, Subcutaneous fat area; V/S, Visceral fat to subcutaneous fat ratio