Published in final edited form as:

Am J Clin Oncol. 2017 June ; 40(3): 277–282. doi:10.1097/COC.0000000000000150.

Oncologic and Functional Hazards of Obesity among Patients with Locally Advanced Rectal Cancer Following Neoadjuvant Chemoradiation Therapy

In J Park, MD, PhD¹, Y. Nancy You, MD, MHSc¹, John M Skibber, MD¹, Miguel A Rodriguez-Bigas, MD¹, Prajnan Das, MD, MS, MPH², Cathy Eng³, Scott Kopetz, MD, PhD³, Robert A Wolff, MD³, Christopher H Crane, MD², Sunil Krishnan, MD², Bruce Minsky, MD², Chung-Yuan Hu, MPH, PhD¹, Sa Nguyen, MS¹, and George J Chang, MD, MS¹

¹Department of Surgical Oncology, the University of Texas, MD Anderson Cancer Center

²Department of Radiation Oncology, the University of Texas, MD Anderson Cancer Center

³Department of Gastrointestinal Medical Oncology the University of Texas, MD Anderson Cancer Center

Abstract

Objective—Obesity is a major health concern and risk factor for colorectal cancer that may also impact cancer treatment and outcomes. Rectal cancer response to chemoradiotherapy (CXRT) is associated with long-term survival and sphincter preservation. The purpose of this study was to evaluate the impact of obesity on treatment outcomes after neoadjuvant CXRT for rectal cancer.

Methods—A retrospective cohort study of patients diagnosed (1993–2010) with cT3-4 or cN+ (by EUS, CT, or MRI) rectal carcinoma and treated with CXRT and TME was performed. Patients were classified as obese (BMI ≥ 30 kg/m²) or non-obese (BMI < 30 kg/m²), and by response to CXRT: complete (ypCR) or incomplete (ypIR). Associations between obesity, tumor response, and sphincter preservation were evaluated using multivariate logistic regression analysis and survival outcomes by Cox regression.

Results—753 patients met criteria and 28.7% (n=216) patients were obese. Obese and non-obese groups did not differ in age, gender, tumor location, grade, or number of examined lymph nodes. However, obesity was associated with a lower rate of ypCR (OR_{multi}=0.60; 95% CI:0.38–0.94, *p*=.04) and among mid-to-low rectal cancer patients, a lower rate of sphincter preservation (OR_{multi}=.67; 95% CI:.45 to .99). Both among obese and non-obese patients, CR was associated with more favorable recurrence-free survival than iCR.

Conclusions—Considering the increasing obesity prevalence and its association with CXRT response, oncologic outcomes, and sphincter preservation, further study is needed regarding the impact of obesity on neoadjuvant treatment response. Moreover, obesity should be targeted as a modifiable risk factor for adverse outcomes following multimodality treatment for rectal cancer.

Keywords

Obesity; rectal cancer, neoadjuvant therapy; biomarker prognosis

Introduction

Obesity is an increasingly prevalent health issue in the United States, currently affecting more than 30% of the population¹. Body mass index (BMI) is one measure of obesity and increased body mass index (BMI) has been shown to be a risk factor for colorectal cancer.^{2–5} Obesity is a particular problem for colorectal surgery, especially in men who are more likely to have visceral obesity, as the adipose tissue can obscure the anatomic dissection planes or limit access to the pelvis. Among patients with rectal cancer, this can result in a particular technical challenge for surgical resection.⁶ As a result, obesity has been associated with an increased risk for perioperative complications and, among patients undergoing primary surgical resection without neoadjuvant therapy, a higher risk for recurrence and decreased likelihood for sphincter preservation.⁷

The current multidisciplinary treatment standard for patients with locally advanced rectal cancer includes preoperative chemoradiotherapy followed by surgery. Preoperative chemoradiotherapy has been associated with significant tumor regression and the potential for improved sphincter preservation.^{8–11} The response of primary rectal cancer to preoperative chemoradiotherapy varies among patients with complete response (pCR) occurring in 15–20%. pCR is an early marker of tumor response, and is associated with favorable prognosis with improved outcomes including local control, distant recurrence, disease-free survival, and overall survival.^{9,12,13} Such findings have clinical relevance both for prognosis and for future treatment stratification. Although many investigators have sought to identify molecular markers that might predict tumor response to preoperative chemoradiotherapy, validated molecular signatures have yet to be identified.^{14,15} In contrast, there has been little investigation of potentially modifiable clinical parameters that may predict tumor response to preoperative chemoradiotherapy.

Previous studies have shown associations between obesity and increased technical difficulty that could increase the morbidity and adversely affect the outcomes after rectal cancer surgery^{16–18}. Although lower rates of sphincter preservation have been reported in obese patients, whether obesity influences sphincter preservation is controversial.^{7,19,20}

We have previously shown that in our cohort of patients, tumor response to neoadjuvant chemoradiotherapy is a short term response indicator of long-term oncologic outcomes¹³. We therefore sought to evaluate the impact of obesity on treatment response, sphincter preservation, and long-term outcomes. We hypothesized that obesity had an adverse impact on oncologic and functional outcomes among patients with rectal cancer.

Methods

Patient Identification

A retrospective cohort study was performed of patients with biopsy proven locally advanced (cT3-4 or cN+ by EUS, CT, or MRI) rectal cancer treated with preoperative chemoradiotherapy followed by radical resection at the University of Texas MD Anderson Cancer Center between 1993 and 2010. Patients were identified from the institutional colorectal cancer patient database and tumor registry. Patients with concurrent distant metastasis at diagnosis or those who were not treated with preoperative chemoradiotherapy, or those with concurrent inflammatory bowel disease, hereditary colorectal cancer syndromes, concurrent malignancy, urgent surgery, prior history of immunotherapy or radiotherapy to the pelvis, prior history of malignancy other than non melanoma skin or in situ cervical cancer were excluded. Patients who lacked information to determine BMI were also excluded. This study was approved by the University of Texas MD Anderson Institutional Review Board.

Assessment of obesity

Body mass index (BMI) was determined for each patient based on patient height and weight information collected from the medical record at the visit before start of preoperative chemoradiotherapy. BMI was calculated as weight (kg) divided by height² (m²), and groups were separated into obese (BMI ≥ 30 kg/m²), and non-obese (BMI < 30 kg/m²) as described by the World Health Organization criteria for obesity^{1,20}.

Clinical staging, treatment and pathologic evaluation

All patients also underwent physical examination including full colonoscopic evaluation to exclude synchronous tumors and proctoscopic evaluation to identify the tumor distance from the anal verge. Pretreatment clinical primary tumor staging was obtained by computed tomography (CT) and magnetic resonance imaging (MRI), or endorectal ultrasound (EUS). Patient and tumor specific variables including clinical stage, pathological stage, histologic grade, total number of involved and examined lymph nodes were analyzed. Tumor location was recorded as distance to the distal-most extent of the tumor from the anal verge but categorized as upper, mid, or low rectum for the purpose of analysis. The radiotherapy was delivered with a median dose of 50.4 Gy, and concurrent chemotherapy which was mainly infusional 5-fluorouracil (5-FU) or capecitabine. Operations were classified as sphincter preserving (low anterior resection or proctectomy with coloanal reconstruction) or non-sphincter preserving (abdominoperineal resection) and were performed with adherence to TME principles. This included proximal vascular ligation of the inferior mesenteric artery with inferior mesenteric vein ligation at the inferior border of the pancreas.

The primary oncologic endpoint was rate of pathologic complete response. Pathologic staging of the resected specimen was performed by dedicated gastrointestinal cancer pathologists in accordance with the guidelines of the College of American Pathologists. The gross tumor volume was entirely embedded and serially sectioned for standard hematoxylin and eosin staining and microscopic evaluation. The mesorectum was manually dissected for lymph nodes, which were then examined with 1–3 separate sections per node. Complete

response was defined as absence of viable adenocarcinoma cells in the surgical specimen (ypT0N0) and could include the presence of acellular mucin pools without viable tumor cells. All other patients were classified as incomplete response.

A planned subgroup analysis for the secondary oncologic endpoints of overall survival (OS), recurrence-free survival (RFS), and local recurrence (LR) was performed among patients with at least 2 years of follow-up. Overall survival was defined as the time from the time of surgery to death from any cause. Recurrence-free survival (RFS) was defined at the time of surgery to tumor recurrence or death from any cause.

Statistical analysis

Patients and tumor related variables were characterized using descriptive statistics and comparisons were performed using the chi square test for proportions. Nonparametric predictor variables were compared using the Wilcoxon rank sum test. Univariate associations between clinical factors at diagnosis and BMI categories were analyzed using logistic regression. Covariate adjusted analyses between BMI categories and outcome variables were performed using multivariate logistic regression to calculate adjusted odds ratios with 95% confidence intervals (CI). P values <0.05 were considered statistically significant. All analyses were performed using SPSS (ver 12.0, SPSS Inc., Chicago, IL).

Results

Patient and tumor characteristics

A total of 753 patients met study criteria and were analyzed. Four-hundred sixty-six were men (61.9%). Median age at time of diagnosis was 58 years (interquartile range (IQR); 49–66). The median BMI of the entire cohort was 27 (IQR; 24–30.8) kg/m² and 216 patients (28.7%) were classified as obese. Median tumor distance from the anal verge was 5 cm (IQR; 5–8 cm). Tumors were located in the upper rectum (>10cm from the anal verge) in 51 (6.7%), mid rectum (6–10 cm from the anal verge) in 315 (41.8%), and low rectum (<5cm from the anal verge) in 388 (51.5%). The overall rate of sphincter preservation was 70.5 %. There were no significant differences between the obese and non-obese patients with respect to age, gender, clinical stage, histologic grade, or total number of examined lymph nodes in the surgical specimen. Total radiation dose and type of concurrent preoperative chemotherapy also did not differ by obesity status. The overall proportion of obese patients increased over time as did the overall rate of sphincter-preserving resections (Table 1).

Pathologic treatment response

The overall rate of pCR following preoperative CXRT for the entire cohort was 17.8% (n=134). The rate of pCR was significantly lower among obese patients than non-obese patients (13.4% vs. 19.6%, $P=.04$). We further examined the influence of BMI on tumor response to neoadjuvant CXRT after adjusting for other potential predictors of tumor response including location, grade, sex, clinical stage, and period of diagnosis. Despite covariate adjustment, the rate of pCR to neoadjuvant CXRT was significantly lower among obese patients with a 40% lower odds for pCR among obese compared to non-obese patients (odds ratio [OR]=0.60; 95% CI, 0.38 to 0.94) (Table 2).

Survival and Recurrence

After a median follow-up of 66 months (IQR, 39– 66 months), rates of local and distant recurrence were evaluated. Differences in overall rates of local or distant recurrence between the obese and non-obese patients were not observed after adjustment for age, sex, tumor location, use of adjuvant chemotherapy, and period of diagnosis. A total of 628 patients (83.4%) received adjuvant chemotherapy but this did not affect RFS. However, among both the obese and non-obese patients, RFS was significantly associated with treatment response (Figure 1).

Sphincter Preservation

Overall, 70.5 % of the patients underwent a sphincter preserving operation. The proportion of patients undergoing sphincter preserving surgery did increase during the study period. This occurred despite the fact that the proportion of obese patients also increased ($P=.02$) (Figure 2). Therefore, patients were stratified by tumor location; then after adjusting for age, gender, tumor response to neoadjuvant CXRT, T4 status, and year of operation, obesity was associated with a 33% lower odds of sphincter preservation ($OR_{adj}=0.67$; 95% CI, 0.45–0.99) among patients with mid and distal rectal cancers, although the effect was primarily associated with tumors located between 5–10 cm from the anal verge (92.2% vs 82.5%, $OR_{adj}=0.34$; 95% CI, 0.13–0.88). However, the most significant factor for sphincter preservation was clinical T4 status ($OR_{adj}=0.17$; 95% CI, 0.09–0.31).

Discussion

The increasing trends in obesity prevalence in the U.S. population and worldwide is an important healthcare problem²¹. In this cohort study of 753 rectal cancer patients treated at a single comprehensive cancer center, higher baseline BMI was associated with lower rates of complete tumor response to neoadjuvant chemoradiotherapy, and among men, an increased risk for overall mortality and local failure. It was also associated with an increased need for permanent colostomy. There has been increasing evidence that tumor response to neoadjuvant chemoradiotherapy is an early indicator of long-term outcomes^{9,13}. Furthermore, response to neoadjuvant chemoradiotherapy may be an important determinant for sphincter preservation. Thus, the lower rate of response to neoadjuvant chemoradiotherapy among obese patients may both signal poorer long-term outcomes and contribute to a lower rate of sphincter preservation.

Obesity has been previously observed to be associated with lower rates of local control and sphincter preservation but less treatment-related toxicity among patients with stage II and III rectal cancer treated with post-operative chemoradiotherapy⁷. Higher BMI has also been observed to be a risk factor for recurrence following adjuvant chemotherapy among patients with colon cancer²¹. However, tumor responses associated with neoadjuvant chemoradiotherapy can potentially mitigate some of these detrimental effects by improving resection margin status and sphincter preservation among patients treated with adherence to TME principles^{8,20}. Yet the observation that obesity is associated with less tumor regression in both men and women further shows that the effects of obesity on patients undergoing curative treatment of rectal cancer are multi-faceted. Indeed, obese patients were 38% less

likely to achieve a pCR than non-obese even after adjusting for covariate effects such as cT, cN, age, location, gender, tumor grade and year of diagnosis. There are a number of potential explanations for this observation including difficulty in delivering optimal radiotherapy to obese patients due to issues related to difficulty with patient positioning. Obese patients may have altered drug and metabolite availability at the tissue level⁷. Moreover, clinical practice patterns have suggested that up to 40% of obese patients may not receive chemotherapy doses that are based on full body weight, suggesting that under-treatment may be an additional factor influencing outcomes^{22,23}. Additionally, biological factors likely exist, such as the association between insulin resistance related to visceral obesity and promotion of cellular proliferation and inhibition of apoptosis in part through an increase in circulating free IGF-1²⁴ or obesity-associated inflammation and subsequent activation of the Wnt pathway. The Wnt-activated phenotype has been demonstrated to be resistant to both chemotherapy and radiation²⁵.

Regardless of the exact mechanisms of the lower rates of neoadjuvant treatment response among obese patients, we observed a clear relationship between treatment response as an early response indicator and long-term recurrence free survival in both the obese and non-obese patients¹⁰. There was no apparent interaction between obesity and treatment response as a predictor of recurrence risk. Obese patients who achieved a pathologic CR still had improved oncologic outcomes when compared to patients who did not achieve a CR. However, fewer obese patients achieved pCR, although due to the relatively small proportion of obese patients who would have been affected by pCR status, our study sample was too small to show a survival difference among the overall cohorts of obese and non-obese.

Obesity itself does not preclude sphincter preservation for patients with low rectal cancer. We observed that despite an increasing proportion of patients over time who were obese, the overall rate of sphincter preservation also increased. However, the rate of increase in the proportion of obese patients was significantly higher than the rate of increase in the proportion of patients undergoing sphincter preservation and the increased risk for permanent colostomy associated with obesity was the greatest among patients with tumors between 5–10 cm from the anal verge (17.5% vs 7.8%, $p=0.029$). The lack of observed association for more distal tumors may suggest that for the most distal tumors, oncologic issues such as sphincter involvement are the primary determinant whereas for tumors between 5–10 cm from the anal verge, other factors such as both the anatomic limitations of a deep, narrow pelvis in obese patients and lower rates of tumor regression may limit the ability to perform sphincter preserving surgery.

This study has both potential limitations and strengths. As inherent in single-institutional retrospective observational cohort studies, there remains the potential for both referral and selection bias. However, the proportion of obese patients ($BMI \geq 30 \text{ kg/m}^2$) in this cohort was 28.9%, comparable to the 1999–2008 National Health and Nutritional Examination Survey report of 33.9%¹. But as noted, there were greater proportions of younger and male patients with more distal and advanced tumors than would have been expected in a general population of patients with rectal cancer. Such bias should not have affected the rate of response to neoadjuvant therapy but these male patients with more advanced distal tumors were more likely to be affected by factors associated with higher BMI when performing

sphincter preserving surgery. It is increasingly recognized that other measures of more accurately classifying visceral obesity than BMI may be more representative of the important factors at play.^{19,26} Despite the large total sample size, the relatively small number of patients affected by the differences in pCR did not have a significant impact on RFS comparisons between the obese and non-obese patients. However, to our knowledge, this is the first study to evaluate the relationship between obesity status and pathologic response to neoadjuvant CXRT among patients with locally advanced rectal cancer. These effects were likely, at least in part, attributable for the lower rates of sphincter preservation and higher rates of local failure particularly among obese men. This was also a relatively long study inclusion period (17 years). However, the majority of the operations were performed in more recent years and by a dedicated colorectal surgical team who were early adopters of both neoadjuvant treatment approaches, TME surgery, and colo-anal reconstruction for rectal cancer. Similarly the pathologic evaluation was performed by dedicated GI pathologists. Moreover improvements in imaging technology for radiation treatment planning (e.g. CT based simulation since 2000) should have resulted in improved delivery of radiotherapy in the latter part of the study when the proportion of obese patients was greater, further supporting our findings. Studies should continue to explore the relationship between obesity and tumor response. However where pCR and sphincter preservation are relevant endpoints in studies of neoadjuvant treatment, BMI may be an important stratifier in the analysis.

Although obesity continues to grow as an increasingly prevalent clinical problem within the US, it is also a largely modifiable health risk. Our data reveal that BMI ≥ 30 kg/m² is associated with both oncologic and functional hazards with lower rates of tumor response to neoadjuvant treatment and sphincter preservation among men and women and higher risk for mortality with a potentially higher rate of local failure in men. Considering the increasing prevalence of obesity, clinicians and public health care policy makers should continue to target obesity as an important modifiable risk factor for treatment outcomes in patients with rectal cancer.

Acknowledgments

Source of Funding: Supported by the National Institutes of Health/National Cancer Institute grants K07-CA133187 (G.J.C.) and CA016672 (MD Anderson Cancer Center's Support Grant).

References

1. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. *Jama*. 2010; 303(3):235–241. [PubMed: 20071471]
2. Giovannucci E, Ascherio A, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Physical activity, obesity, and risk for colon cancer and adenoma in men. *Ann Intern Med*. 1995; 122(5):327–334. [PubMed: 7847643]
3. Le Marchand L, Wilkens LR, Mi MP. Obesity in youth and middle age and risk of colorectal cancer in men. *Cancer Causes Control*. 1992; 3(4):349–354. [PubMed: 1617122]
4. Pischon T, Lahmann PH, Boeing H, et al. Body size and risk of colon and rectal cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). *J Natl Cancer Inst*. 2006; 98(13):920–931. [PubMed: 16818856]
5. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet*. 2008; 371(9612):569–578. [PubMed: 18280327]

6. You JF, Tang R, Changchien CR, et al. Effect of body mass index on the outcome of patients with rectal cancer receiving curative anterior resection: disparity between the upper and lower rectum. *Ann Surg.* 2009; 249(5):783–787. [PubMed: 19387325]
7. Meyerhardt JA, Tepper JE, Niedzwiecki D, et al. Impact of body mass index on outcomes and treatment-related toxicity in patients with stage II and III rectal cancer: findings from Intergroup Trial 0114. *J Clin Oncol.* 2004; 22(4):648–657. [PubMed: 14966087]
8. Sauer R, Fietkau R, Wittekind C, et al. Adjuvant versus neoadjuvant radiochemotherapy for locally advanced rectal cancer. A progress report of a phase-III randomized trial (protocol CAO/ARO/AIO-94). *Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ...[et al].* 2001; 177(4):173–181.
9. Rodel C, Martus P, Papadoupolos T, et al. Prognostic significance of tumor regression after preoperative chemoradiotherapy for rectal cancer. *J Clin Oncol.* 2005; 23(34):8688–8696. [PubMed: 16246976]
10. Chang GJ, Park I, You YN, et al. Neoadjuvant treatment response and outcomes in locally advanced rectal cancer: Establishing oncologic benchmarks. *J Clin Oncol.* 2011; 29(S15)
11. Sauer R, Becker H, Hohenberger W, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. *N Engl J Med.* 2004; 351(17):1731–1740. [PubMed: 15496622]
12. Maas M, Nelemans PJ, Valentini V, et al. Long-term outcome in patients with a pathological complete response after chemoradiation for rectal cancer: a pooled analysis of individual patient data. *Lancet Oncol.* 2010; 11(9):835–844. [PubMed: 20692872]
13. Park I, You YN, Agawal A, et al. Neoadjuvant Treatment Response as an Early Response Indicator for Patients with Rectal Cancer. *J Clin Oncol.* 2012; 30 In press.
14. Ghadimi BM, Grade M, Difilippantonio MJ, et al. Effectiveness of gene expression profiling for response prediction of rectal adenocarcinomas to preoperative chemoradiotherapy. *J Clin Oncol.* 2005; 23(9):1826–1838. [PubMed: 15774776]
15. Watanabe T, Komuro Y, Kiyomatsu T, et al. Prediction of sensitivity of rectal cancer cells in response to preoperative radiotherapy by DNA microarray analysis of gene expression profiles. *Cancer Res.* 2006; 66(7):3370–3374. [PubMed: 16585155]
16. Bege T, Lelong B, Francon D, Turrini O, Guiramand J, Delpero JR. Impact of obesity on short-term results of laparoscopic rectal cancer resection. *Surg Endosc.* 2009; 23(7):1460–1464. [PubMed: 19116737]
17. Benoist S, Panis Y, Alves A, Valleur P. Impact of obesity on surgical outcomes after colorectal resection. *Am J Surg.* 2000; 179(4):275–281. [PubMed: 10875985]
18. Ishii Y, Hasegawa H, Nishibori H, Watanabe M, Kitajima M. Impact of visceral obesity on surgical outcome after laparoscopic surgery for rectal cancer. *Br J Surg.* 2005; 92(10):1261–1262. [PubMed: 16078294]
19. Moon HG, Ju YT, Jeong CY, et al. Visceral obesity may affect oncologic outcome in patients with colorectal cancer. *Ann Surg Oncol.* 2008; 15(7):1918–1922. [PubMed: 18392660]
20. Chern H, Chou J, Donkor C, et al. Effects of obesity in rectal cancer surgery. *J Am Coll Surg.* 2010; 211(1):55–60. [PubMed: 20610249]
21. Dignam JJ, Polite BN, Yothers G, et al. Body mass index and outcomes in patients who receive adjuvant chemotherapy for colon cancer. *J Natl Cancer Inst.* 2006; 98(22):1647–1654. [PubMed: 17105987]
22. Sinicrope FA, Foster NR, Yoon HH, et al. Association of obesity with DNA mismatch repair status and clinical outcome in patients with stage II or III colon carcinoma participating in NCCTG and NSABP adjuvant chemotherapy trials. *J Clin Oncol.* 2012; 30(4):406–412. [PubMed: 22203756]
23. Lyman GH. Impact of chemotherapy dose intensity on cancer patient outcomes. *J Natl Compr Canc Netw.* 2009; 7(1):99–108. [PubMed: 19176210]
24. Frystyk J, Vestbo E, Skjaerbaek C, Mogensen CE, Orskov H. Free insulin-like growth factors in human obesity. *Metabolism.* 1995; 44(10 Suppl 4):37–44. [PubMed: 7476310]
25. Eyler CE, Rich JN. Survival of the fittest: cancer stem cells in therapeutic resistance and angiogenesis. *J Clin Oncol.* 2008; 26(17):2839–2845. [PubMed: 18539962]

26. Siegel EM, Ulrich CM, Poole EM, Holmes RS, Jacobsen PB, Shibata D. The effects of obesity and obesity-related conditions on colorectal cancer prognosis. *Cancer Control*. 2010; 17(1):52–57. [PubMed: 20010519]

Figure 1.

Recurrence-Free survival according to response to neoadjuvant CXRT: A) Among non-obese patients. Incomplete response was associated with lower RFS rate (HR, 2.4; 95% CI, 1.42–4.04) B) Among obese patients, patients with incomplete response showed shorter RFS (HR, 3.36; 95% CI, 1.04–10.85)

Figure 2.
Trends in proportion of patients obese (lower line) and those undergoing sphincter preserving operation (upper line) over time

Table 1

Clinical and tumor characteristics of the patients(%)

Characteristics	Non-obese	Obese	P
N *	537(71.3)	216(28.7)	
BMI, kg/m ² *	25.3[22.9–27.4]	33.4[31.5–37.1]	
Age *	57[49–67]	58[49–66]	0.91
Gender			0.78
Male	334(62)	132(61)	
Female	203(38)	84(39)	
Location(from anal verge)			0.52
>10 cm	34(6.2)	17(7.9)	
6–10 cm	230(42.8)	85(39.4)	
5 cm	274(51.0)	114(52.8)	
Clinical T			0.77
cT2	27(5.0)	9(4.2)	
cT3	437(81.4)	176(81.5)	
cT4	49(9.1)	18(8.3)	
Unknown	24(4.5)	13(6.0)	
Clinical N			0.87
cN negative	212(39.5)	87(40.3)	
cN positive	281(52.3)	110(50.9)	
Unknown	44(8.2)	19(8.8)	
Concurrent chemotherapy			0.49
Pyrimidine-based agent	457(85.1)	185(85.6)	
Others(including combination)	80(14.9)	31(14.4)	
Radiation dose *	50.4[45–52.5]	50.4[45–52.5]	0.60
Sphincter preserving surgery	387(72.1)	144(66.7)	0.14
Grade			0.39
Well-moderately differentiated	461(85.5)	182(84.3)	
Poorly-undifferentiated	55(10.2)	27(12.5)	
Unknown	21(4.3)	7(3.2)	
Pathologic tumor response			0.04
Complete remission(pCR)	105(19.6)	29(13.4)	
Incomplete remission(IR)	432(80.4)	187(86.6)	
Total No. lymph nodes assessed *	11[6–17]	13[8–17.5]	0.12
Diagnostic period **			0.06
1993–2001	256(74.6)	87(25.4)	
2002–2010	281(68.5)	131(31.5)	

* Median values with interquartile range[IQR],

** Row percentage

Table 2

Factors associated with pathologic response to neoadjuvant chemoradiotherapy

variables	Univariate		Multivariate	
	Odds ratio	95%CI	Odds ratio	95% CI
Obesity				
No, BMI <30	1		1	
Yes, BMI ≥ 30	0.64	0.41–0.99	0.60	0.38–0.94
Location				
>10 cm from anal verge	1		1	
6–10 cm from anal verge	0.38	0.22–0.66	0.36	0.20–0.62
5cm from anal verge	0.46	0.28–0.76	0.47	0.28–0.78
Sex				
Male	1			
Female	1.03	0.7–1.51		
Tumor grade				
Low (G1, G2)	1		1	
High (G3, G4)	0.79	0.42–1.47	1.19	0.67–2.13
cT stage				
cT2+cT3	1		1	
cT4	0.34	0.13–0.87	0.41	0.15–1.06
cN stage				
N negative	1		1	
N positive	1.18	0.80–1.74	0.94	0.81–1.81
Period				
1993–2001	1		1	
2002–2010	1.26	0.86–1.84	1.16	0.78–1.71

CI, Confidence interval

Table 3

Factors associated with sphincter preservation among patients with mid-distal rectal cancer (n=703)

Variable	Univariate		Multivariate	
	Odds ratio	95% CI	Odds ratio	95% CI
Obesity				
No, BMI <30	1		1	
Yes, BMI ≥ 30	0.72	0.49–1.05	0.67	0.45–0.99
Tumor response				
IR	1		1	
CR	1.50	0.91–2.47	1.34	0.80–2.27
Gender				
Male	1		1	
Female	1.04	0.75–1.45	1.12	0.77–1.64
Age				
<50	1		1	
50–75	1.12	0.76–1.66	1.10	0.73–1.66
>75	0.56	0.26–1.03	0.47	0.23–.98
cT4 stage				
No	1		1	
Yes	0.17	0.09–0.32	0.17	0.09–0.31
Period				
1993–2001	1		1	
2002–2010	1.64	1.19–2.32	1.64	1.14–2.37

CI, Confidence interval