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ORIGINAL ARTICLE

Impact of intra-peritoneal fat distribution on intra-operative bleeding volume with D2 lymphadenectomy in Chinese patients with gastric cancer

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Summary *Objective:* To explore the quantitative measurements and evaluation of intra-peritoneal fat distribution by MDCT and its significance in predicting intra-operative bleeding volume during D2 lymphadenectomy in gastric cancer (GC) patients.
Methods: From June 2016 to September 2017, GC patients scheduled for open gastrectomy with D2 lymph-node dissection were enrolled. According to the BMI, the subjects were then classified as normal BMI(BMI<25 kg/m^2); overweight (BMI = 25–30 kg/m^2) and obese (BMI≥30 kg/m^2). According to the intraoperative blood loss (IBL), the patients were further separated into high IBL (IBL; ≥ 300 ml) or low IBL (<300 ml). Clinicopathological parameters between the groups were statistically compared and univariate and multivariate analysis were used to identify predictive factors such as intra-peritoneal fat areas (IFA) and intra-peritoneal fat areas ratio (IFAR) for high IBL.
Results: A total of 226 patients were included in the study where 53 patients underwent distal while 173 underwent total gastrectomy. According to the BMI classification, there were 25 normal BMI, 108 overweight and 25 obese subjects. According to the IBL, there were 98 high IBL and 128 low IBL subjects. IFA and IFAR were significantly greater in the high IBL group than in the low IBL group. There was no significant difference in any other clinicopathological factors between the high IBL group and the low IBL group. Multivariate analysis revealed that high IFA and IFAR independently predicted high IBL.
Conclusion: The use of MDCT to evaluate the precise distribution of abdominal fat during preoperative examination can prompt surgeons to develop techniques to decrease intraoperative bleeding in obese patients. Nevertheless, it is yet necessary to be surgically more meticulous when dealing with patients with high IFA or high IFA/IFAR in order to improve the outcome of D2 gastrectomy.

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1. Introduction

Obesity is associated with substantial intraoperative technical difficulties and increased patient morbidity after open gastrectomy.[1–10] Body mass index (BMI) is a widely accepted indicator of obesity. Higher BMI is related to prolonged operating time, increased intra-operative bleeding and a lower count of dissected lymph nodes.[11–16] However, the BMI is yet not the most accurate reflection of the distribution of intra-peritoneal fat since the distribution of fatty tissue differs greatly between individuals, especially different ethnicities, races or areas for that matter.[17] In China, gastrectomy with D2 lymph node dissection is a well-developed and widely accepted procedure for the treatment of gastric cancer.[18] However, this standardized procedure still has technical challenges when it comes to patients with higher degree of visceral fat accumulation. Over the recent years, several techniques have been developed to assess the visceral fat distribution. In terms of reproducibility and accuracy, computed tomography (CT) is proved to be the optimal technique for assessing visceral fat[19] when compared with alternatives such as ultrasonography,[20] magnetic resonance imaging (MRI)[21] and other anthropometric measurements.[22,23] Several studies have shown that the intra-peritoneal fat area (IFA) determined from a single scan at the level of the umbilicus is closely correlated with the total volume of visceral fat.[24,25] Hence, using the IFA to assess the degree of visceral fat, intra-abdominal fat could reveal the challenges to the surgical approach during the pre-operative evaluation. It is commonly known that the volume of intra-operative bleeding is related to the complexity of the surgical technique and it has been reported that in abdominal procedures such as gastrectomy for Gastric Cancer, the distribution of visceral fat would eventually affect the surgical procedure.[25–29] In this study, we have investigated the relationship between intra-operative bleeding volume and individual fat parameters (intra-abdominal fat areas and ratio) in order to pre-evaluate the complexity of the surgical approach in patients with abdominal fat undergoing open approach gastrectomy.

2. Patients and methods

2.1. Patients

From June 2016 to September 2017, patients scheduled for open gastrectomy, whether distal or total with curative intent (R0 resection) admitted in the Ward 3 of the Department of General Surgery Ward of Ruijin Hospital were included for this study. Patients who had previous history of abdominal intervention or surgery or previous course of chemotherapy or radiotherapy were excluded.

2.2. CT protocol

MDCT examination was performed by using a 4-detecor row CT scanner (Light Speed, QXI; GE Medical System, Milwaukee, WI). After fasting more than 8hrs, each patient had received an intramuscular injection of 20 mg anisodamine to decrease the peristaltic bowel movement and 10—15 min before scanning, the patients were asked to drink 1—1.5 L of water to allow proper expansion of the stomach. 100 ml bolus of nonionic iodine contrast agent (Ultravist; Schering, Germany) was injected at the speed of 3 ml/s through antecubital vein by an automatic intravenous injector with 20 ml gauge needle during the enhanced scan phase. Another 80 ml bolus of contrast agent was subsequently administered at the speed of 1 ml/s. CT acquisitions were performed in the arterial phase (first 30sec), the portal venous phase (75sec later) and the equilibrium phase (180sec later). With the section thickness of 5 mm, all CT data were transferred to a workstation (Advantage Workstation 4.2 G.E.) for multi-planar reconstruction (MPR) images by one radiologist. CT scanning parameters were as

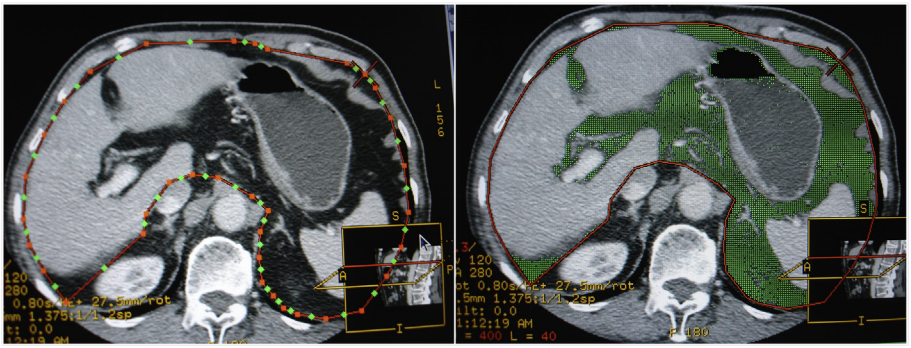

Fig. 1 Distribution of intra-peritoneal fat as measured by Advantage Workstation 4.2 G.E. on a CT scan at the portal vein level. The visceral fat area was regarded as green.

follows: 4-detecor rows used; pitch, 3; reconstruction interval 2.5 mm; 200 Ma; 120 KV and tube rotation time 0.8 sec.

2.3. Evaluation of intra-peritoneal adipose area

Intra-peritoneal fat and its components were calculated using histogram software during the equilibrium phase. Adipose tissue was defined as any area with Hounsfield intensity of between −250 and −50 HU. Intra-peritoneal fat areas (IFA) and Intra-peritoneal fat area ratio (IFAR, Intra-peritoneal fat areas/total abdominal fat areas) were measured at the slice level of the portal vein (Fig. 1).

2.4. Clinical characteristics

All operations were performed or supervised by the same surgical team with extensive experience of open gastrectomy and one experienced pathologist was employed to ensure quality consistency of pathological diagnosis. Lymph node dissection extents followed recommendations of the Japanese Research Society for Gastric Carcinoma.[19] The staging and definition of lymph nodes were principally based on the 8th edition of the International Union Against Cancer (UICC) TNM staging classification.[20]

The potential effects of clinical characteristic factors, eg., age, sex, BMI, on early surgical outcomes defined in terms of intra-operative blood loss, operating time, number of retrieved lymph nodes, duration of hospital stay after surgery, and postoperative complication (pneumonia, postoperative bleeding, wound infection, anastomotic leakage, sepsis and deep vein thrombosis). In order to precisely assess the effect of BMI on open gastrectomy, the patients were classified into three groups: a normal BMI group (BMI$<$25 kg/m^2); an overweight group (BMI $=$ 25−30 kg/m^2) and an obese groups (BMI$\geq$30 kg/m^2) according to the BMI classification from World Health Organization (WHO). The patients' characteristics, intra-operative parameters and postoperative parameters were compared within these three groups.

Intra-operative blood loss was measured by reading the volume of blood in the suction bottle and weighing gauze swabs soaked before and after surgery. To assess the influence of intra-abdominal adipose on open gastrectomy, the patients were divided into two groups according to IBL: a high IBL group (IBL$\geq$300 ml) and a low IBL group (IBL$<$300 ml). Operating time was recorded by the anaesthesiologist as the time from skin incision till completion of skin closure. Anastomotic leakage was diagnosed by radiological examination using orally administered contrast media. The patients' characteristics, intra-operative parameters and postoperative parameters were compared within these two groups.

2.5. Statistical analysis

Statistical analyses were performed with SAS'PROC GLM' software version 9.0 for Windows (SAS Institute, Cary, NC, USA). The quantitative data was presented as mean ± SD and evaluated with the Student's t-test and analysis of variance (ANOVA). The qualitative data were evaluated with Chi-square test and Fisher's exact test. A multivariate logistic regression analysis was performed subsequently to identify the variables such as age; gender; tumor location; Borrmann's type; tumor size; histological type; depth of invasion; lymph-node metastasis; operative procedure; stapler or not; BMI; IFA and IFAR that were considered to have effect on the intra-operative blood loss. All variables (both significant and insignificant variables by univariate analysis) were included in the multivariate analysis. A P-value of less than 0.05 was considered to indicate a statistically significant difference.

3. Results

From June 2016 to September 2017, 226 gastric cancer patients scheduled for open gastrectomy, whether distal or total with curative intent (R0 resection) were included for this study. There were 146 male and 80 female aged between 27 and 90 years old. There were 62 patients with early gastric carcinoma (EGC) and 164 with advanced gastric carcinoma (AGC). 53 patients underwent total gastrectomy with D2 lymphadenectomy. The remaining 173 underwent distal subtotal gastrectomy with D2 lymphadenectomy.

When classified into 3 groups according to the BMI, there were 108 patients in the were normal BMI group (BMI$<$25 kg/m^2); 93 patients in the overweight group (BMI $=$ 25−30 kg/m^2) and 25 patients in the obese group (BMI$\geq$30 kg/m^2). There were no differences in any clinicopathological factors among the obesity group, overweight group and the normal BMI group (Table 1). The mean intra-operative blood loss (IBL) was 345.2 ± 273.7 ml. When divided according to IBL, the high IBL group (IBL$\geq$300 ml) comprised of 98 patients while the low IBL group (IBL$<$300 ml) comprised of 128. Also the operating time, the IBL, the number of dissected lymph nodes and the complication did not differ among these three groups. No mortality occurred in the patients (Table 2). The IFA and the IFAR were significantly greater ($p < 0.001$) in the high IBL group than those in the low IBL group. There were no differences in any other clinicopathological factors (Table 3). Also the surgical outcomes did not differ between the two groups. Hospital death was not observed among the patients (Table 4).

The multivariate analysis including IFA, IFAR along with the other eleven variables described above showed that IFA and IFAR independently affected high IBL ($p < 0.001$ and OR $= 1.001$, $p = 0.004$ and OR $= 1.343$, respectively; Table 5).

4. Discussion

Gastrectomy with D2 lymph node dissection is considered technically more difficult and challenging in patients with more localized intra-abdominal fat where the second-level lymph nodes are usually embedded, hence significantly influencing with the efficiency of the lymphadenectomy. BMI is an indicator of obesity, and higher BMI seems to be related to increased morbidity and mortality rates.[1,2,14–16] However, it is calculated simply from the patient's height and weight and is hence not a precise reflection of the intra-abdominal fat area and distribution.

Table 1 Patient characteristics and BMI undergoing open gastrectomy with D2 lymph-node dissection for gastric cancer.

	Normal BMI (n = 108)	Overweight (n = 93)	Obesity (n = 25)	p-value
Age(y)	60.4 ± 10.7	60.4 ± 13.4	59.0 ± 11.0	0.861
Gender				0.630
Male	70	62	14	
Female	36	33	11	
IFA (cm^2)	7270.8 ± 4166.5	7592.3 ± 4252.9	6318.2 ± 3834.3	0.398
IFA/TFA	39.1 ± 8.3	40.0 ± 7.7	37.2 ± 8.1	0.276
Tumor location				0.071
U	16	16	1	
M	19	6	4	
L	71	73	20	
Tumor size (mm)	50.1 ± 35.8	52.7 ± 32.5	51.1 ± 31.4	0.946
Histological type				0.086
tubular adenocarcinoma	45	46	6	
signet-ring cell carcinoma	25	18	12	
papillary adenocarcinoma	12	5	2	
mucinous adenocarcinoma	14	19	3	
other	10	7	2	
Depth of invasion				0.854
T1	30	19	7	
T2	20	19	5	
T3	42	46	10	
T4	14	11	3	
Lymph-node metastasis				0.621
N0	54	39	11	
N1	32	39	9	
N2	10	12	3	
N3	10	5	2	
Stage				0.900
IA	27	22	5	
IB	11	8	3	
IIA	11	9	2	
IIB	11	9	2	
IIIA	21	24	8	
IIIB	11	15	3	
IIIC	14	8	2	
Stapler				0.333
Yes	98	90	25	
No	8	5	0	
Operative procedure				0.463
Distal gastrectomy	77	73	21	
Total gastrectomy	29	22	4	

Table 2 Surgical outcomes and BMI undergoing open gastrectomy with D2 lymph-node dissection for gastric cancer.

	Normal BMI (n = 108)	Overweight (n = 93)	Obesity (n = 25)	p-value
Age(y)	60.4 ± 10.7	60.4 ± 13.4	59.0 ± 11.0	0.861
operating time (min)	243.6 ± 63.1	233.5 ± 73.2	228.4 ± 66.0	0.451
Retrieved lymph nodes	27 (15—67)	23 (14—78)	22.5 (13—53)	0.509
Intra-operative blood loss (ml)	249.5 ± 67.4	254.1 ± 75.4	238.0 ± 39.8	0.949
Complication				0.394
Presence	11	11	5	
absence	97	82	20	
Hospital death	0	0	0	

Table 3 Patient characteristics and IBL undergoing open gastrectomy with D2 lymph-node dissection for gastric cancer.

	High IBL (n = 98)	Low IBL (n = 128)	p-value
Age(y)	60.4 ± 13.4	59.0 ± 11.0	0.861
Gender			0.635
Male	65	81	
Female	33	47	
IFA (cm^2)	11107.0 ± 2487.1	4381.3 ± 2503.2	<0.001
IFA/TFA	45.1 ± 4.8	34.8 ± 7.1	<0.001
Tumor location			0.264
U	25	23	
M	39	49	
L	34	56	
Tumor size (mm)	59.2 ± 15.6	54.9 ± 22.5	0.109
Histological type			0.591
tubular adenocarcinoma	34	51	
signet-ring cell carcinoma	23	32	
papillary adenocarcinoma	11	9	
mucinous adenocarcinoma	12	25	
other	8	11	
Depth of invasion			0.078
T1	22	40	
T2	19	22	
T3	38	55	
T4	19	11	
Lymph-node metastasis			0.959
N0	44	60	
N1	35	45	
N2	12	13	
N3	7	10	
Stage			0.694
IA	19	35	
IB	10	12	
IIA	11	12	
IIB	10	11	
IIIA	23	30	
IIIB	12	17	
IIIC	13	11	
Stapler			0.311
Yes	93	117	
No	5	11	
Operative procedure			0.523
Distal gastrectomy	73	100	
Total gastrectomy	25	28	

Although the relationship between visceral fat area and hypertension/glucose intolerance has been well documented,[12] there is still lack of more precise tools to efficiently provide surgeons with a pre-operative image of the anatomical distribution of visceral abdominal fat during the evaluation stage. Hence, in the present study, abdominal imaging by MDCT permitted a precise calculation of the individual fat areas. This study revealed that a high IFA and IFAR adversely affected the high IBL in open gastrectomy with D2 lymph-node dissection.

Gastric cancer is one of the most common malignancies In China. Due to the changes in the standards of living and lifestyle, there has been an increased rate of obesity in the Chinese population. With researches pointing out the risk of gastric cancer increasing with obesity, there is significantly a higher probability of surgeons having to operate on obese patients with more intra-abdominal fat content, hence increasing the rate of intraoperative and post-operative morbidity.[1,2] Nevertheless, there have been other reports suggesting that high BMI had no effect on undesirable surgical outcomes of open gastric surgery.[26–30] The current study evaluated the surgical outcomes of open gastrectomy with D2 lymph-node dissection for gastric cancer according to BMI. But this study failed to reveal this relationship between BMI and the IBL. A recent report revealed that the VFA/body surface area might be a more useful index than the BMI for predicting the technical difficulties involved in laparoscopic resection of rectosigmoid carcinoma.[30] The current study showed that high IFA and IFAR could independently predict high IBL. The volume of IBL was thought to be greater in the high IFA and IFAR group because fatty tissue has more abundant blood vessels; leakage from the

Table 4 Surgical outcomes and IBL undergoing open gastrectomy with D2 lymph-node dissection for gastric cancer.

	High IBL (n = 108)	Low IBL (n = 98)	p-value
Age(y)	60.4 ± 10.7	60.4 ± 13.4	0.861
operating time (min)	243.6 ± 63.1	233.5 ± 73.2	0.451
Retrieved lymph nodes	27 (15—67)	23 (14—78)	0.509
Complication			0.193
Presence	15	8	
absence	93	90	
Hospital death	0	0	1

Table 5 Logistic regression analysis was performed to evaluate predictive factors for high IBL.

Variable	Odds ratio (95%CI)	p value
Age	1.010 (0.965—1.058)	0.665
gender	0.988 (0.276—3.529)	0.985
Tumor location	1.529 (0.311—7.524)	0.602
Borrmann's type	1.624 (0.868—3.040)	0.129
Tumor size	1.396 (0.930—2.097)	0.108
Histological type	0.743 (0.430—1.283)	0.286
Depth of invasion	0.817 (0.355—1.881)	0.634
Lymph-node metastasis	0.932 (0.417—2.083)	0.863
Operative procedure	0.360 (0.018—7.230)	0.505
Stapler	0.174 (0.010—2.998)	0.229
BMI	0.987 (0.799—1.218)	0.899
IFA	1.001 (0.998—1.143)	<0.001
IFA/TFA	1.343 (1.171—1.583)	0.0004

fatty tissue might thus have accounted for the relatively high blood loss. These results suggest that the IFA is a useful predictive factor for high IBL in open gastrectomy D2 lymph-node dissection.

An excess of fat tissue necessitates more complex lymphnode dissection and a larger operation area, which can sometimes be associated with haemorrhaging. More delicate haemostatic manipulation is thus necessary in obese patients to reduce the volume of IBL.

5. Conclusion

The use of MDCT to evaluate the precise distribution of abdominal fat during preoperative examination can prompt surgeons to develop techniques to decrease intraoperative bleeding in obese patients. Nevertheless, it is yet necessary to be surgically more meticulous when dealing with patients with high IFA or high IFA/TFAin order to improve the outcome of D2 gastrectomy.

Conflict of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.asjsur.2018.11.008.

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