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Article

Prognostic Impact of Visceral Fat Area Measured by Bioelectrical Impedance Analysis on Oncologic Outcomes of Colorectal Cancer

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Abstract: Purpose: Some studies showed that increase of visceral fat was associated with post-operatively clinical outcomes and oncologic outcomes. However, to our knowledge, there were no studies about using BIA to find the effects of visceral fat on oncologic outcomes of CRC. The purpose of this study was to investigate the relationship between the visceral fat area (VFA) and clinical, nutritional, and oncologic outcomes in patients with colorectal cancer (CRC); **Methods**: The study included 203 patients who underwent anthropometric measurement by bioelectrical impedance analysis (BIA) before surgical treatment for CRC between January 2016 and June 2020; **Results:** According to the cut-off level of VFA by receiver operating characteristic curve analysis: 85 (40.5%) patients had a low VFA, and 119 (59.5%) patients had a high VFA. Preoperative C-reactive protein (CRP) in the high VFA group was significantly higher than that in the low VFA group (0.8±1.7 vs. 0.4±0.7, p=0.047). There was no significant difference in the overall perioperative outcomes including total operation time, time to gas out, sips of water, and soft diet, hospital stay, and morbidity between the two groups. The proportion well-differentiated adenocarcinoma in the low VFA group was statistically significantly higher than in the high VFA group (11.9% vs. 2.6%, p=0.027). Nutritional prognostic factors including platelet-lymphocyte ratio, neutrophil-lymphocyte ratio, platelet-lymphocyte index, and pan-immune inflammation value and body composition data including skeletal muscle index and phase angle, and body fluid were not significantly different between the two groups. Multivariate analysis found that preoperative CRP (hazard ratio [HR], 3.882; 95% confidence interval [CI], 1.001 to 15.051; p=0.050) and nodal stage (HR, 7.996; 95% CI, 1.414 to 45.209; p=0.019) were independent prognostic factor for overall survival and the sex (HR, 0.110; 95% CI, 0.013 to 0.905; p=0.040), lymphovascular invasion (HR, 3.560; 95% CI, 1.098 to 11.544; p=0.034) and VFA (HR, 4.263; 95% CI, 1.280 to 14.196; p=0.040) were independent prognostic factors for disease-free survival; **Conclusion:** high visceral fat adiposity preoperatively measured by BIA was associated with higher preoperative CRP and was independent prognostic factor for DFS.

Keywords: colorectal neoplasm; nutrition assessment; body composition; electric impedance; prognosis

1. Introduction

Colorectal cancer (CRC) is the third most frequently diagnosed cancer and the second most common cause of mortality worldwide [1]. According to the World Health Organization, 39% of adults aged ≥ 18 years are overweight, and 13% of adults are obese [2]. Obesity is now a well-established risk factor for the development of colorectal cancer and is associated with an increase in CRC-related mortality [3]. The underlying mechanisms correlating obesity with CRC have not been completely elucidated, but sustained inflammatory signaling, chronic insulin resistance, adipokine dysregulation induced by adipose tissue macrophages, and hypoxic and angiogenic environments of obese adipose tissue with elevated circulating cytokines have been proposed as important factors for carcinogenesis [4].

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The body mass index (BMI) is one of the most reliable anthropometric methods for detecting obesity [5], however it has no bearing on the accumulation of adipose tissue, particularly intraabdominal or visceral fat tissue [6]. Controversies exist regarding the correlation between visceral obesity and colon cancer outcomes. Some studies have shown that visceral obesity is associated with poorer clinical and oncologic outcomes, including longer hospital stays, higher morbidity within 30 days, longer operation times, more aggressive pathologic tumor features, and poorer survival rates [7,8]. However, other studies have reported that visceral obesity has a protective effect on overall survival compared to non-visceral obesity [9,10].

Analysis of body composition describes the proportions of fat, protein, and minerals in human bodies. Bioelectrical impedance analysis (BIA) is a noninvasive technique that is cost-effective and available at many healthcare services for nutritional assessment and anthropometric analysis, including percentages of fat, protein, body fluid, and minerals in human bodies. Previous studies have shown the relationships between body composition, including sarcopenia, using skeletal muscle index, visceral fat, phase angle, and clinical and oncologic outcomes of CRC [11,12]. However, to date, no studies have investigated the effects of visceral fat on the clinical, pathological, and oncologic outcomes of CRC using BIA. Therefore, our study aimed to compare the impact of visceral fat measured using BIA on clinical, pathologic, and oncologic outcomes in patients who underwent surgical treatment for CRC.

2. Materials and Methods

2.1. Patients and data collection

This study was approved by the Institutional Review Board of the Dongsan Medical Center (Daegu, Republic of Korea, IRB No. 2022-07-015). The need for informed consent was waived due to the retrospective nature of this study. Between January 2016 and June 2020, 204 patients who underwent laparoscopic surgery for colorectal cancer were included in the study group. Exclusion criteria included concurrent or prior malignancies, malignancies other than adenocarcinoma, familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (Figure 1).

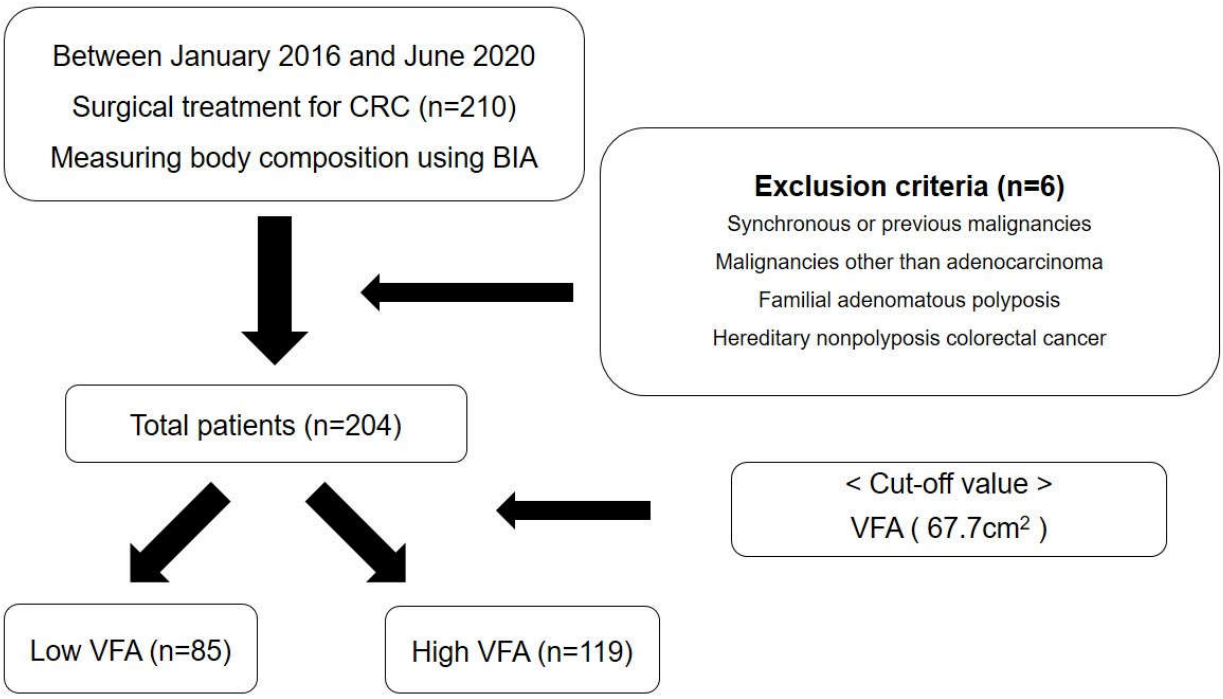

Figure 1. Flow chart of the exclusion criteria.

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2.2. Data collection and definitions

A prospectively maintained database and electronic medical records were searched to collect the data. Data on patient demographics, including age, sex, American Society of Anesthesiology (ASA) score, preoperative carcinoembryonic antigen (CEA), BMI, and location of the tumor and immune and inflammation biomarkers, including platelet-lymphocyte ratio (PLR), neutrophil-lymphocyte ratio (NLR), prognostic nutritional index (PNI), and pan-immune inflammation value (PIV) were collected retrospectively using electronic medical records. Perioperative outcomes included operation time, time to gas out, sips of water, soft diet, hospital stay, morbidity within 30 days, and Clavien–Dindo classification. Pathological outcomes included tumor, node, metastasis (TNM) stage, histology, number of harvested lymph nodes and positive lymph nodes, tumor size, lymphovascular invasion, and perineural invasion from medical records. Body composition also included phase angle, appendicular skeletal muscle mass (ASM), skeletal muscle index (SMI), and body fluid, intracellular fluid, extracellular fluid, and body fat mass measured using BIA. The eighth edition of the American Joint Committee on Cancer classification system was utilized to identify pathological tumor depth, the number of lymph nodes with metastases, and cancer stage. During each 3-year follow-up examination, a postoperative clinical examination, measurement of serum CEA levels, chest radiography every 3 months, and chest/abdominal CT every 6 months were conducted. After three years, the period between follow-ups was reduced to six months. Recurrence was defined as the radiologically or histologically confirmed existence of tumor. Local recurrence was defined as any tumor recurrence within the surgical field; local recurrence accompanied by synchronous systemic recurrence was considered systemic recurrence. Overall survival (OS) was defined as the interval between the date of surgery and the date of the most recent follow-up visit or the date of death from any cause, whereas disease-free survival (DFS) was defined as the interval between the date of surgery and the date of any recurrence.

2.3. Preoperative evaluation and surgical treatment

All patients underwent preoperative evaluations including colonoscopy, computed tomography of the chest and abdomen, and magnetic resonance imaging of the pelvis. Some patients were scanned using positron emission tomography to determine the presence of distant metastases. For CRC, we adhered to the general principles of mesocolic or mesorectal excision and central vessel ligation. The original tumor was removed by performing a precise dissection of the visceral plane from the parietal fascia layer and removing the entire regional mesocolon in one piece.

2.4. Bioelectrical impedance analysis

Inbody 770 (Biospace, Republic of Korea) was utilized to assess the patient's body composition at their initial visit. We classified variables as body composition and metabolic index, fat index, muscle index, obesity index, and phase angle, among other BIA parameters. SMI was calculated using Baumgartner's definition (appendicular/height^2).

2.5. Assessment of hematologic parameters and inflammation-based prognostic scores

Just prior to surgery, blood samples were drawn from patients as part of preoperative work-up to examine hematologic parameters such as hemoglobin, white blood cell (WBC), hemoglobin, platelet, and albumin. A complete blood cell count was performed on these blood samples to calculate the PLR, NLR, PNI, and PIV. The PLR was determined by dividing the absolute number of platelets by the absolute number of lymphocytes. A cut-off value of 150 was utilized to split patients into low and high PLR groups [9]. Other inflammation-based prognostic scores were also computed (prognostic nutritional index [PNI]: 10× serum albumin concentration (g/dL) + 0.005 × absolute lymphocyte count; NLR: absolute neutrophil count/absolute lymphocyte count). The PIV is a new biomarker that includes neutrophils, lymphocytes, platelets, and monocyte, and preoperative PIV was

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calculated using the following formula (absolute neutrophil count × platelet count × absolute monocyte count / absolute lymphocyte count) [13].

2.6. Statistical analysis

For continuous outcomes, the findings are provided as means with standard deviation ranges, and for categorical outcomes, as frequencies with percentages. Chi-square and Fisher's exact tests were used to assess categorical variables. The t-test and Mann-Whitney test were used to evaluate continuous variables. A p-value of 0.05 or less was regarded as statistically significant. Because of the asymptotic distribution of our data, the optimal cutoff value of visceral fat area (VFA) in our study was estimated using the Contal and O'Quigley method [14]. In survival analysis, the Contal and O'Quigley approach is used to discover cut-off points in continuous variables. The method involves calculating all log-rank statistics and picking the ideal cut point based on the log-rank statistic's maximum value. This procedure was applied to every conceivable cutoff, and the one with the highest Q statistic was chosen for further examination. Events of the Contal and O'Quigley equations were included in mortality and recurrence.

Using the log-rank test for univariate analysis, the Kaplan-Meier method was used to examine the OS and the DFS curve. To determine if adiposity influences DFS, Cox proportional hazards models were utilized. Individual variables' effects on patient survival were reported as hazard ratios (HRs) with 95% confidence intervals (CIs). The statistical studies were conducted using version 25 of IBM SPSS Statistics (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Baseline characteristics of patients

We defined the cutoff values of VFA based on DFS using the Contal and O'Quigley method. VFA ≥ 67.7 cm^2 was defined as high VFA. Based on these cutoff values, 85 (41.7%) patients had low VFA and 119 (58.3%) patients had high VFA. The patient and tumor characteristics according to low and high adiposity are shown in Table 1. The percentage of men was higher in patients with low VFA than in those with high VFA (77.6% vs. 62.2%; p = 0.019). Patients with high VFA showed higher preoperative C-reactive protein (CRP) and BMI than patients with low VFA (0.8 ± 1.7 vs. 0.4 ± 0.7, p = 0.047 and 25.0 ± 2.6 vs. 21.3 ± 1.8; p < 0.001, respectively). There were no significant differences in age, preoperative CEA level, ASA class, and tumor location between the two groups. Immune-inflammatory prognostic markers, including PLR, NLR, PNI, and PIV, showed no significant differences between the two groups.

Table 1. Patient and Tumor Characteristics.

	Low VFA (n=85)	**High VFA** (n=119)	**p value**
Age (year)	65.9±9.7	66.0±10.2	0.929
Sex			0.019
Male	66 (77.6)	74 (62.2)	
Female	19 (22.4)	45 (37.8)	
Preoperative CEA (ng/mL)	7.0±20.7	5.4±16.0	0.552
Preoperative CRP	0.4±0.7	0.8±1.7	0.047
ASA groups			0.827
I	26 (30.6)	33 (27.7)	
II	49 (57.6)	69 (58.0)	
III	26 (30.6)	33 (27.7)	
BMI (kg/m^2)	21.3±1.8	25.0±2.6	<0.001

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Location of tumor			0.599
Right	22 (25.9)	27 (22.7)	
Left	63 (74.1)	92 (77.3)	
Hemoglobin (g/dl)	12.6±2.0	12.4±1.7	0.609
Platelet (x10^3)	246.2±71.8	241.4±72.3	0.636
WBC (x10^3)	6.4±2.1	6.0±1.9	0.105
PLR	181.7±114.6	188.2±102.2	0.677
NLR	3.3±3.8	3.1±2.5	0.636
PNI	66.9±27.7	71.2±30.8	0.305
PIV	383.1±710.2	276.9±294.7	0.196
Albumin (g/dl)	4.2±0.5	4.2±0.4	0.603

Values are presented as mean ± standard deviation or number (%). ASA: American society of anesthesiologists; BMI: Body mass index; CEA: Carcinoembryonic antigen; CRP: C-reactive protein; NLR: Neutrophil lymphocyte ratio; PIV: Pan-immune inflammation value; PLR: Platelet-lymphocyte ratio; PNI: Prognostic nutritional index; VFA: Visceral fat area; WBC: White blood cell.

3.2. Perioperative clinical outcomes

Table 2 demonstrates that there is no significant difference between the low and high VFA groups in terms of overall perioperative outcomes, including operation time, time to gas out, sips of water, soft food, and hospital stay. There were no statistically significant differences in morbidity 30 days after surgery and the proportion of patients with Clavien-Dindo classification > 3a.

Table 2. Perioperative Clinical Outcomes.

	Low VFA (n=85)	**High VFA** (n=119)	**p value**
Operation time (min)	209.3±112.1	204.0±86.2	0.711
Time to gas out (d)	3.2±2.2	4.0±4.8	0.319
Time to sips of water (d)	4.0±3.1	4.0±4.8	0.983
Time to soft diet (d)	6.3±3.2	6.6±5.1	0.603
Time to hospital stay (d)	10.4±6.4	10.2±6.2	0.773
Morbidity within 30 days after surgery	28 (32.9)	40 (33.6)	0.920
Clavien-dindo classifications > 3a	17 (20.0)	25 (21.0)	0.861

Values are presented as mean±standard deviation or number (%). d: day; min: minute; VFA: visceral fat area.

3.3. Postoperative pathologic outcomes

Table 3 shows postoperative pathologic outcomes. There were no significant differences in tumor and nodal stage, number of retrieved lymph nodes, proportion of patients with more than 12 lymph nodes acquired, number of positive lymph nodes, tumor size, lymphovascular invasion, and perineural invasion between low and high VFA groups. Patients with high VFA showed more moderate and poor differentiation than patients with low VFA (90.6% vs. 83.3% and 6.8% vs. 4.8%; p = 0.027).

Table 3. Postoperative Pathologic Outcomes.

	Low VFA (n=85)	**High VFA** (n=119)	**p value**

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Tumor stage			0.114
T1	16 (18.8)	33 (24.0)	
T2	16 (18.8)	42 (20.6)	
T3	43 (50.6)	99 (48.5)	
T4	10 (11.8)	14 (6.9)	
Nodal stage			0.945
N0	55 (64.7)	79 (66.4)	
N1	21 (24.7)	27 (22.7)	
N2	9 (10.6)	13 (10.9)	
Histology			0.027
Well differentiated	10 (11.9)	3 (2.6)	
Moderately differentiated	70 (83.3)	106 (90.6)	
Poorly differentiated	4 (4.8)	8 (6.8)	
Retrieved LNs	19.5±9.4	18.1±9.2	0.310
LN > 12	77 (90.6)	99 (83.2)	0.130
Positive LNs	1.0±2.0	0.9±2.1	0.807
Tumor size (cm)	3.9±2.1	3.5±2.1	0.211
Lymphovascular invasion	27 (31.8)	27 (23.5)	0.192
Perineural invasion	16 (19.3)	25 (22.5)	0.584

Values are presented as mean ± standard deviation or number (%). LN: Lymph node; VFA: Visceral fat area

3.4. Body composition analysis using BIA

Table 4 shows the body composition analysis of patients with low and high VFA using BIA. Patients with high VFA had higher weight compared to patients with low VFA (66.2 ± 11.2 vs. 56.4 ± 7.8; p = 0.001). Other body components, such as phase angle, appendicular skeletal muscle mass, and skeletal muscle index, did not differ statistically between the two groups. Body fluid, intracellular fluid composition, and extracellular fluid composition did not differ significantly between the two groups; however, the high VFA group had a larger body fat mass (20.3 ± 4.8 vs. 11.6 ± 2.6; p＜0.001).

Table 4. Inbody 770 Body Composition Analysis of Patients.

	Low VFA (n=85)	**High VFA** (n=119)	**p value**
Height (cm)	162.3±8.6	162.4±9.5	0.980
Weight (kg)	56.4±7.8	66.2±11.2	<0.001
Phase angle (')	5.1±0.6	5.0±0.7	0.629
ASM (kg)	7.0±1.1	7.1±1.1	0.650
SMI (kg/m^2)	2.7±0.5	2.7±0.4	0.749
Body fluid	33.1±5.3	33.9±6.7	0.347
ICF (%)	20.3±3.4	20.8±4.2	0.362
ECF (%)	12.8±2.0	13.1±2.6	0.328
BFM (kg)	11.6±2.6	20.3±4.8	<0.001

Values are presented as mean±standard deviation or number(%). ASM: Appendicular skeletal muscle mass; BFM = Body fat mass; ECF: Extracellular fluid; ICF: Intracellular fluid; SMI: Skeletal muscle index; VFA: Visceral fat area.

3.5. Oncologic outcomes

The median follow-up period was 35.6 months in the low VFA groups and 40.0 months in the high VFA group, without significant differences. The high VFA group

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showed poor prognosis in 5-year OS and DFS, but there were no statistical differences (88.3% vs. 90.3%; p=0.909 and 79.8% vs. 89.3%; p = 0.105). There were three cases of recurrence in the low VFA group and 14 cases of recurrence in the high VFA group. All recurrences were included as systemic recurrence in the low VFA group, but nine cases of systemic recurrence and five cases of local recurrence developed in the high VFA group. In the low VFA group, two patients had liver recurrence and one patient showed peritoneal seeding. Three patients showed liver recurrence, three patients showed lung recurrence, one patient showed bone metastasis and two patients showed peritoneal seeding. Figure 2 shows the relationship between VFA and long-term survival using the Kaplan–Meier curve. OS and DFS were better in patients with low VFA, without statistical differences (OS 90.3% vs. 88.3%; p = 0.909, DFS 89.3% vs. 79.8%; p = 0.095) (Figure 2).

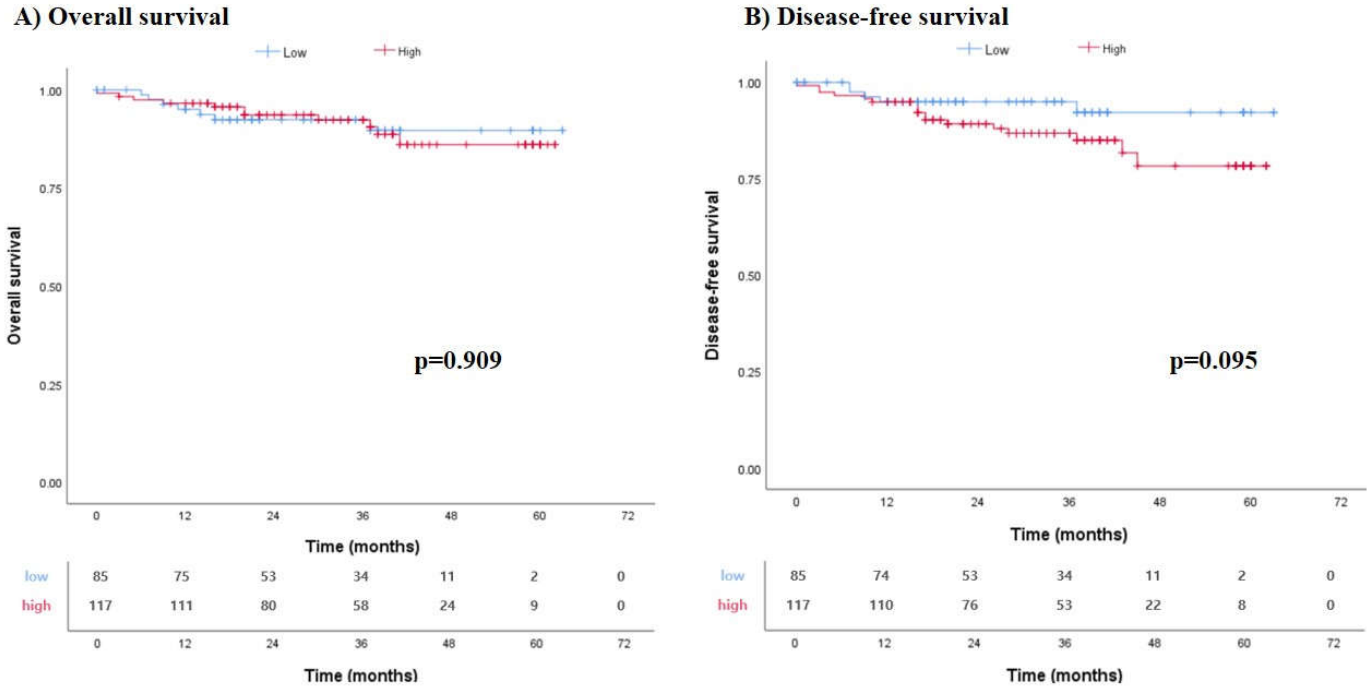

Figure 2. Kaplan-Meier survival curve for the cumulative risk of recurrence. Kaplan-Meier survival curve showed better overall survival (p = .909) and disease-free survival (p =.095) without significant difference in patients with low visceral fat area, respectively.

3.6. Univariate and multivariate survival analyses of prognostic factors

Univariate analyses revealed that preoperative CRP level, lymph nodal status, perineural invasion, and PIV were significant prognostic factors for OS (Supplementary Figure 1). Sex, tumor and nodal status, and perineural invasion were identified as significant prognostic factors for DFS (Supplementary Figure 2). Multivariate analysis found that preoperative CRP (HR, 3.882; 95% CI, 1.001–15.051; p=0.050) and nodal stage (HR, 7.996; 95% CI, 1.414–45.209; p=0.019) were independent prognostic factors for OS, while sex (HR, 0.110; 95% CI, 0.013–0.905; p=0.040), lymphovascular invasion (HR, 3.560; 95% CI, 1.098–11.544; p=0.034), and VFA (HR, 4.263; 95% CI, 1.280–14.196; p=0.040) were independent prognostic factors for DFS.

4. Discussion

This study demonstrated that high visceral fat adiposity preoperatively measured by BIA was associated with higher preoperative CRP levels and poorer histologic differentiation in patients with CRC who underwent curative resection. In the multivariate analysis

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of oncologic outcomes, visceral fat was an independent prognostic factor for DFS. In contrast, VFA was not significantly linked with short-term clinical and pathological outcomes, immune-inflammatory prognostic indicators, or other body compositions, including skeletal muscle index, body fluid, and phase angle.

Several studies have shown that the operation time is longer, and postoperative complications occur more frequently after surgery in patients with high VFA [7,8]. A recent meta-analysis that aimed to determine the impact of VFA on laparoscopic CRC surgery showed that visceral obesity was associated with increased surgical difficulty and postoperative morbidity [15]. However, another recent study concluded that there was no significant relationship between visceral fat, intraoperative difficulties, and postoperative complications [16]. In this study, there were no significant differences in perioperative short-term outcomes, including total operation time, recovery-related outcomes, or postoperative complications, between patients with low and high VFA. We believe that factors other than visceral obesity had a greater impact on perioperative outcomes in our study. Future research will require further studies, such as multivariate analysis of perioperative outcomes.

Elevated CRP is a well-known risk factor for several cancers and has poor prognostic value in colorectal cancers [17]. In the present study, preoperative elevated CRP level was associated with high VFA and was investigated as an independent poor prognostic factor for OS, in line with previous studies. Previous studies have shown a significant correlation between CRP levels and visceral adiposity [18,19]. Based on previous research and our own findings, visceral adipose tissue is suggested to be associated with chronic cancer inflammation.

Several studies have produced contradictory findings regarding the clinical significance of visceral fat in relation to oncologic outcomes. Park et al. reported that patients with high VFA showed less lymph node metastasis or lower metastatic lymph node ratio; however, there was no association between VFA and the OS of CRC patients [10]. In contrast, other studies have found a significant association between a high VFA and poor oncologic outcomes [20,21]. In the current study, univariate analysis revealed no statistically significant differences between the high and low VFA groups in terms of oncologic outcomes; however, multivariate analysis revealed the VFA as an independent prognostic factor for DFS. In general, female sex is a well-known prognostic factor for colorectal cancer [22]. Our study showed that female sex was an independent prognostic factor for DFS with an HR of 0.11 compared to male sex. In the univariate analysis, the prognostic impact of VFA on DFS was offset by female sex being a good prognostic factor in women. However, in multivariate analysis, the prognostic impact of VFA was analyzed as an independent poor prognostic factor.

Several investigations have demonstrated the importance of visceral obesity to the development of cancer and the function of omental fat in intraperitoneal carcinogenesis, which was associated with the systemic recurrence of CRC [23,24]. Park et al. showed an association between higher visceral adipocytes and a higher risk of peritoneal seeding in recurrent colorectal cancer [25]. Regarding mechanisms of colorectal cancer development, previous research demonstrated that visceral adipocytes contained elevated levels of inflammatory lipid metabolism markers, some of which were associated with CRC tumor stage, and that obesity-induced chronic low-grade inflammation induces oxidative stress factors [8,26]. 4-Hydroxynonenal (HNE) is the primary result of lipid peroxidation and is responsible for deregulation of several pathways involved in cell proliferation and differentiation, cell survival, apoptosis, and necrosis. The molecular pathways mainly altered by 4-HNE include the mitogen-activated protein kinase, phosphatidylinositol 3-kinase (PI3KCA)/protein kinase B (AKT) signaling pathway, and nuclear factor kappa B (NF-κB). Moreover, accumulation of DNA mutations, such as APC, KRAS, NRAS, BRAF, or PIK3CA, makes obesity a multifactor phenomenon involved in CRC initiation and progression[8].

Numerous studies have investigated the effect of visceral fat composition on the clinical and oncological outcomes of colorectal cancer using dual-energy X-ray

absorptiometry or CT [7,8,15]. However, measuring the area of visceral fat using CT or DEXA is a time-consuming task and requires a specific program [27]. In contrast, BIA is a noninvasive, cost-effective, and widely accessible method for nutritional evaluation and anthropometric measurements performed by clinicians and health providers. Recently, several studies have established the validity of evaluating body fat composition using BIA against CT scans, and these studies have demonstrated good concordance between BIA and CT scan [28,29]. A prospective cohort study found that a high body fat percentage measured by BIA was associated with an increased risk of advanced CRC tumors, particularly in men [30]. We expect that research on body fat components and colorectal cancer using BIA will continue.

Nevertheless, our study has some limitations. This study had a retrospective design, which bears the issues of incomplete data and potential selection bias in a single-center study. Although our cutoff values may be adequate for Asian ethnic groups, it may be challenging to apply our findings to other ethnic groups. Additionally, the median follow-up period of patients participating in this study was relatively short (35 months for low VFA and 40 months for high VFA), which limits the analysis of long-term oncological outcomes.

5. Conclusion

In conclusion, high visceral fat adiposity preoperatively measured by BIA was associated with higher preoperative CRP levels and was an independent prognostic factor for DFS.

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Table 5. Oncologic Outcomes.

	Low VFA (n=85)	High VFA (n=119)	p value
Median follow-up (months)	35.6±16.2	40.0±18.0	0.073
5-yr OS (%)	90.3	88.3	0.909
5-yr DFS (%)	89.3	79.8	0.105
Recurrence	3	14	
Recurrence pattern			0.070
Systemic recurrence	3	9	
Local recurrence	0	5	

Values are presented as mean±standard deviation or number(%); DFS: disease free survival; OS: Overall survival; VFA: Visceral fat area

Table 6. Prognostic Factors of 5-year Survival by Univariate Analysis.

Prognostic factor	N	OS (5 years, %)	Log Rank p-value	DFS (5 years, %)	Log Rank p-value
Visceral fat area			0.909		0.105
Low	85	90.3		89.3	
High	119	88.3		79.8	
Age			0.689		0.917
≤ 65	89	90.2		84.7	
> 65	115	87.8		82.1	
Sex			0.060		0.016
Male	140	85.5		79.5	
Female	64	96.9		92.0	
BMI			0.332		0.327
High (>25)	52	92.8		90.2	
Low (<25)	152	87.5		80.8	
ASA score			0.253		0.571
1	59	94.9		81.9	
2 & 3	145	86.6		84.0	
Sideness			0.431		0.687
Right sided	49	84.2		79.4	
Left sided	155	90.6		84.7	
Pre-op CEA (ng/ml)			0.164		0.072
< 5	162	90.6		85.0	
≥5	42	82.2		76.7	
Pre-op CRP (mg/l)			0.043		0.623
< 0.3	99	90.0		86.6	
≥0.3	55	80.3		83.7	
Tumor stage			0.119		0.037
T1 & T2	91	92.8		92.0	
T3 & T4	113	85.6		76.0	
Nodal stage			<0.001		0.001
Nodal negative	133	94.5		90.4	
Nodal positive	71	79.0		69.5	
Differentiation			0.822		0.488
Well	15	92.9		92.9	
Moderate & poor	188	89.1		83.0	
Lymphovascular invasion			0.085		0.089
No	146	90.8		84.8	
Yes	54	83.3		78.3	
Perineural invasion			0.030		0.004

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No	153	92.1		85.5	
Yes	41	80.6		72.6	
LN harvest			0.314		0.363
≥12	176	88.3		82.2	
< 12	28	92.3		92.9	
PIV			0.010		0.298
Low	145	94.1		86.1	
High	59	77.3		77.1	
Phase angle			0.215		0.944
Low	117	92.1		85.3	
High	87	84.3		82.4	
Sarcopenia			0.311		0.313
No	143	90.3		85.0	
Yes	61	85.6		79.4	

ASA: American society of anesthesiologists; BMI: Body mass index; CEA: Carcinoembryonic antigen; CRP: C-reactive protein; LN: Lymph node; PIV: Pan-immune inflammation value.

Table 7. Prognostic Factors of Overall Survival and Disease-Free Survival in Multivariate Analysis.

Variables	Reference category	Overall Survival		Disease-free survival	
		HR (95% CI)	p- value	HR (95% CI)	p-value
VFA					
High	Low	1.67 (0.50 – 5.56)	0.401	4.26 (1.28 – 14.20)	0.018
Sex					
Female	Male	0.59 (0.12 – 2.87)	0.509	0.11 (0.01 – 0.91)	0.040
Sarcopenia					
Yes	No	1.57 (0.49 – 5.08)	0.451	2.31 (0.79 – 6.77)	0.126
Pre-OP CEA					
≥5	<5	0.96 (0.29 – 3.16)	0.942	0.92 (0.28 – 3.04)	0.890
CRP					
≥0.3	<0.3	3.88 (1.00 – 15.05)	0.050	1.38 (0.44 – 4.35)	0.585
PIV					
High	Low	1.17 (0.316 – 4.356)	0.811	0.62 (0.19 – 2.03)	0.426
Tumor stage					
T3, T4	T1, T2	0.91 (0.14 – 6.08)	0.926	1.11 (0.27 – 4.63)	0.889
Nodal stage					
N1, N2	N0	8.00 (1.41 – 45.21)	0.019	1.28 (0.37 – 4.45)	0.702
Lymphovascular invasion					
Yes	No	3.06 (0.88 – 10.63)	0.078	3.56 (1.10 – 11.54)	0.034
Perineural invasion					
Yes	No	1.10 (0.31 – 3.95)	0.880	2.46 (0.73 – 8.25)	0.144

CEA: Carcinoembryonic antigen; CRP: C-reactive protein; PIV: Pan-immune inflammation value; VFA: Visceral fat area