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ORIGINAL ARTICLE

Evaluation of preoperative visceral fat area / psoas muscle area ratio and prognosis in patients with colorectal cancer

Nobuhiro Hosoi[1] | Takuya Shiraishi[1] | Takuhisa Okada[1] | Katsuya Osone[1] | Takehiko Yokobori[2] | Makoto Sakai[1] | Hiroomi Ogawa[1] | Makoto Sohda[1] | Ken Shirabe[1] | Hiroshi Saeki[1]

[1]Department of General Surgical Science, Gunma University Graduate School of Medicine, Maebashi, Japan

[2]Division of Integrated Oncology Research, Gunma University, Initiative for Advanced Research (GIAR), Maebashi, Japan

Correspondence
Takuya Shiraishi, Department of General Surgical Science, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi 371-8511, Gunma, Japan.
Email: whity.shiro@gmail.com

Abstract

Background: Recent research has focused on the prognostic relevance of preoperative sarcopenia and sarcopenic obesity in various cancers. In this study we investigated the relationship between visceral fat area (VFA), psoas muscle area (PMA), and the prognosis of patients undergoing colorectal cancer surgery.

Methods: Patients with stage III colorectal cancer who underwent surgery between July 2013 and April 2020 were included. The analysis was performed on 151 patients who met the criteria. The VFA and PMA were measured at the level of the third lumbar vertebra on computed tomography (CT) scans, and the ratio of VFA to PMA (V/P ratio) was determined.

Results: Patients with high V/P ratios were significantly older ($p = 0.0213$), had a higher body mass index (BMI) ($p < 0.0001$), a higher percentage of sarcopenic obesity ($p < 0.0001$), and more diabetes complications ($p < 0.0001$). Prognostic analysis showed that the overall survival (OS) ($p = 0.0154$) and relapse-free survival (RFS) ($p = 0.0378$) were significantly worse in patients with a high V/P ratio. Multivariate analysis revealed that a high V/P ratio was an independent poor prognostic factor for OS. Subgroup analysis was then performed in patients with BMI $< 25\,kg/m^2$. OS ($p = 0.0259$) and RFS ($p = 0.0275$) were significantly worse in the high V/P ratio group. A high V/P ratio was an independent poor prognostic factor in the multivariate analysis.

Conclusion: In colorectal cancer, the preoperative V/P ratio is an independent factor for poor prognosis. Preoperative evaluation of the V/P ratio may identify a wide range of high-risk patients because it is an independent poor prognostic factor in patients without obesity.

KEYWORDS
colorectal cancer, prognosis, psoas muscle, sarcopenic obesity, visceral fat

1 | INTRODUCTION

In recent years, research has been conducted on the relationship between body composition and tumors. Sarcopenia, a concept proposed by Rothenberg,[1] is defined as the loss of skeletal muscle mass and strength that occurs with aging.[2] Sarcopenia has been reported to shorten overall survival (OS), disease-free survival (DFS), and cancer-specific survival (CSS) in colorectal cancer.[3-6]

Sarcopenic obesity is a condition in which obesity is combined with skeletal muscle loss.[7] Increased insulin resistance has been reported to result in activation of tumor cell proliferation signals and poor prognosis.[8-15] Sarcopenic obesity is not clearly defined, and many reports define obesity based on body mass index (BMI).[13,16,17] The prevalence of obesity, defined as a BMI of >30 kg/m^2 in the WHO classification, is lower in Asia than in the West,[18] and so caution is needed when using this definition. In addition, some reports have suggested that fat mass may be a more useful prognostic indicator than BMI.[19] Therefore, it is likely that among patients who fall outside the definition of sarcopenic obesity by BMI, there are patients with poor prognosis who cannot be identified.

We previously reported that the ratio of the psoas muscle area (PMA) to the visceral fat area (VFA) at the level of the third lumbar vertebra (V/P ratio) may be a prognostic factor in esophageal and esophagogastric junction cancer.[20,21] Although the V/P ratio is useful for the preoperative identification of high-risk patients, it has not been reported in colorectal cancer. In this study, we investigated the relationship between the V/P ratio and colorectal cancer prognosis.

2 | METHODS

2.1 | Patients

This was a retrospective study. This study was approved by the Ethics Committee of the Graduate School of Medicine, Gunma University (protocol number: HS2023-097). Informed consent was obtained through an opt-out on the website.

This study included 232 patients with clinical stage III colorectal cancer who underwent colorectal cancer surgery at Gunma University Hospital between July 2013 and April 2020. Of these, 151 patients were analyzed, excluding 19 patients who underwent palliative surgery instead of radical surgery, and 62 patients who were followed up for less than 3 y, excluding those who died (Figure 1).

Medical records were reviewed for age, sex, height, weight, BMI, comorbidities, VFA, subcutaneous fat area (SFA), PMA, psoas muscle index (PMI), pathological stage, serum albumin levels, and postoperative complications within 30 d of surgery. Pathologic stage was classified according to the 8th edition of the TNM classification of the International Union Against Cancer (UICC). Postoperative complications were graded according to the Clavien–Dindo classification. Diabetes mellitus was defined following diagnosis by a specialist and those who were undergoing treatment.

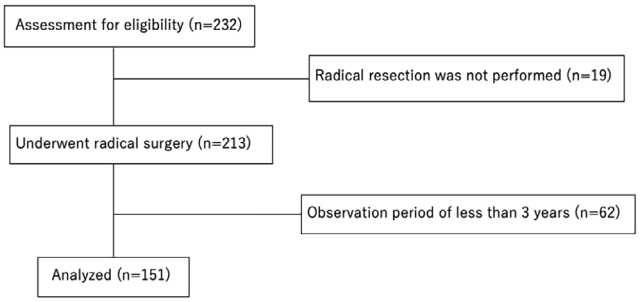

FIGURE 1 Diagram of inclusion and exclusion.

Survival and recurrence rates were investigated, using July 2023 as the final follow-up. Surveillance for recurrence and survival was based on examination and blood sampling every 3 mo, computed tomography (CT) scans every 6 mo, and colonoscopy every year. If recurrence was suspected, a positron emission tomography scan and tissue diagnosis were added to confirm the diagnosis.

2.2 | Definition of sarcopenia, obesity, and sarcopenic obesity

VFA and PMA were measured from CT images of the third lumbar spine vertebral body using a 3D image analysis system (Synapse Vincent v. 5.5, Fujifilm, Tokyo, Japan). Abdominal CT scans obtained within a month before the surgery were used. The V/P ratio was calculated as VFA divided by PMA, following Sakai et al.[20] The CT images of typical cases are shown in Figure 2. The PMI was calculated as the PMA divided by height squared. The PMI cutoffs were set for men at 6.36 cm^2/m^2 and for women at 3.92 cm^2/m^2, based on previous reports.[22,23]

BMI was calculated as the square of height (m) divided by weight (kg), and the definition of obesity was BMI 25 kg/m^2 or higher, as defined by the Japan Society for the Study of Obesity.[18] Sarcopenic obesity was defined as below the PMI cutoff and BMI > 25 kg/m^2.[13]

2.3 | Statistical analysis

Continuous variables were analyzed using one-way analysis of variance, and categorical variables were analyzed using the χ^2 test. The primary endpoint was OS, defined as the date of surgery to the date of death or last follow-up. Relapse-free survival (RFS) was calculated from the date of surgery to the date of cancer recurrence, death, or last follow-up. OS and RFS were assessed using the Kaplan–Meier method. Univariate and multivariate analyses were performed to identify confounding factors. All analyses were performed using the JMP Pro software (v. 15, Cary, NC, USA).

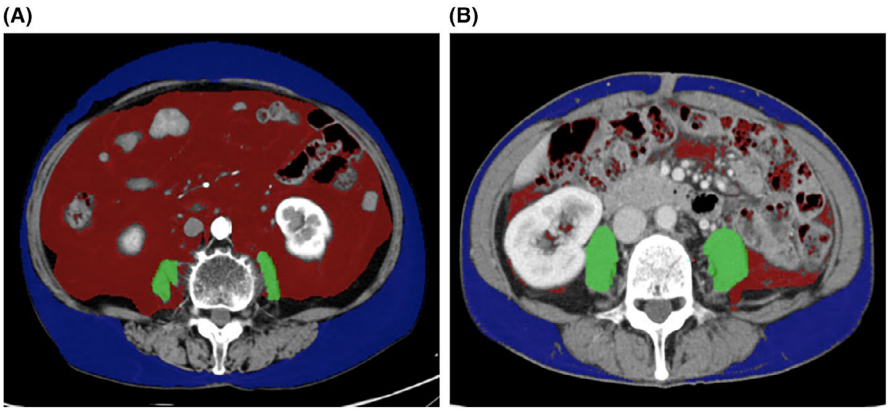

FIGURE 2 CT images of a patient with a typical high V/P ratio and a low V/P ratio. (A) High V/P ratio patient. (B) Low V/P ratio patient. In the figure, blue area is the subcutaneous fat area, red area is the visceral fat area, green area is the psoas muscle area.

TABLE 1 Patient characteristics.

Characteristics	V/P ratio		
	Low ($n = 123$, <13.7)	High ($n = 28$, ≧13.7)	*p*-value
Age, y [mean (SD)]	62.6 (13.1)	68.7 (8.23)	0.0213
Sex (%)			
Female	45 (36.5)	15 (53.5)	0.0974
Male	78 (63.5)	13 (46.5)	
BMI, kg/m^2 [mean (SD)]	22.1 (3.68)	26.0 (4.55)	<0.0001
VFA, cm^2 [mean (SD)]	80.1 (61.5)	195.6 (73.0)	<0.0001
SFA, cm^2 [mean (SD)]	96.9 (59.0)	137.1 (56.7)	0.0013
PMA, cm^2 [mean (SD)]	13.7 (5.58)	11.0 (3.41)	0.0147
PMI, cm^2/m^2 [mean (SD)]	5.15 (1.75)	4.26 (1.07)	0.0113
Albumin, g/dL [mean (SD)]	3.83 (0.55)	3.82 (0.53)	0.9594
Postoperative complication (CD≧II) (%)			
Presence	47 (38.2)	9 (32.1)	0.5485
Absence	76 (61.8)	19 (67.9)	
Tumor location (%)			
Colon	54 (43.9)	19 (67.9)	0.0221
Rectum	69 (56.1)	9 (32.1)	
Pathological stage (%)			
I	13 (10.5)	2 (7.1)	0.5072
II	35 (28.5)	11 (39.3)	
III	75 (61.0)	15 (53.6)	
Postoperative adjuvant chemotherapy (%)			
Presence	72 (58.5)	14 (50)	0.4103
Absence	51 (41.5)	14 (50)	
Sarcopenic obesity (%)			
Presence	4 (3.2)	8 (28.5)	<0.0001
Absence	119 (96.8)	20 (71.5)	
Diabetes mellitus (%)			
Presence	14 (11.3)	13 (46.4)	<0.0001
Absence	109 (88.7)	15 (53.6)	

Abbreviations: BMI, body mass index; CD, Clavien–Dindo classification; PMA, psoas muscle area; PMI, psoas muscle index; SD, standard deviation; SFA, subcutaneous fat area; VFA, visceral fat area.

3 | RESULTS

3.1 | Patient characteristics

The analysis was performed on 151 patients. The median observation period was 59 mo. The best cutoff values for V/P ratio and BMI for OS based on receiver operating characteristic (ROC) curves for all-cause mortality were 13.7 (area under the curve [AUC] 0.52326) and 21.06 (AUC 0.49600), respectively. Based on the cutoff values, 28 patients had a high V/P ratio (≥13.7), and 123 patients had a low V/P ratio (<13.7). The associations with other factors in each group are shown in Table 1.

In the high V/P ratio group, there were four deaths from the primary disease and four deaths from other diseases. Deaths from other diseases included two patients with other cancers, one patient with pneumonia, and one patient with cardiovascular disease. In the low V/P ratio group, there were 13 deaths from the primary disease and five deaths from other diseases. Other disease deaths included two from other cancers, one from peritonitis, one from cerebral infarction, and one from cardiovascular disease.

Analysis of patient characteristics showed that a higher V/P ratio was associated with higher age ($p=0.00213$), higher BMI ($p<0.0001$), higher VFA ($p<0.0001$), higher SFA ($p=0.0013$), higher PMA ($p=0.0147$), higher PMI ($p=0.0113$), more sarcopenic obesity ($p<0.0001$), and more diabetes mellitus ($p<0.0001$). Albumin level, pathological stage, and postoperative complications were not associated with the V/P ratio.

3.2 | Relationship between V/P ratio and prognosis of colorectal cancer

The association of V/P ratio and colorectal cancer prognosis was analyzed (Figure 3). The 3-y survival rate for the observation group was 87.4%. OS ($p=0.0154$) and RFS ($p=0.0378$) were significantly worse in the high V/P ratio group. The 3-y survival rate for the low V/P ratio group was 90.2%, compared to 71.4% for the high V/P ratio group.

In univariate and multivariate analyses, high V/P ratio ($p=0.0365$) and postoperative complications of Clavien–Dindo grade II or higher ($p=0.0116$) were independent poor prognostic factors for OS (Table 2).

3.3 | Significance of the V/P ratio in nonobese patients

The usefulness of the V/P ratio in the group without obesity was also examined. In this study, 35 and 116 patients were classified into the obesity and nonobesity groups, respectively. Subgroup analysis was performed on 116 subjects in the nonobesity group; 14 had a high V/P ratio (≥13.7), and 102 had a low V/P ratio (<13.7) (Table 3). In patients without obesity, higher V/P ratios were associated with higher BMI ($p=0.0090$), VFA ($p<0.0001$), SFA ($p=0.0182$), PMI ($p=0.0282$), and diabetes mellitus complications ($p=0.0003$). Albumin level, pathological stage, and postoperative complications were not associated with the V/P ratio. In the high V/P ratio group, there were four deaths from the primary disease and one death from another cancer. In the low V/P ratio group, there were 12 deaths from the primary disease and five deaths from other diseases; two from other cancers, one from peritonitis, one from cerebral infarction, and one from cardiovascular disease. Prognostic analysis revealed significantly worse OS ($p=0.0259$) and RFS ($p=0.0275$) in the high V/P ratio group (Figure 4). The 3-y survival rate for the low V/P ratio group was 88.4%, compared to 64.3% in the high V/P ratio group.

In univariate and multivariate analyses, high V/P ratio ($p=0.0273$) and postoperative complications of Clavien–Dindo grade II or higher

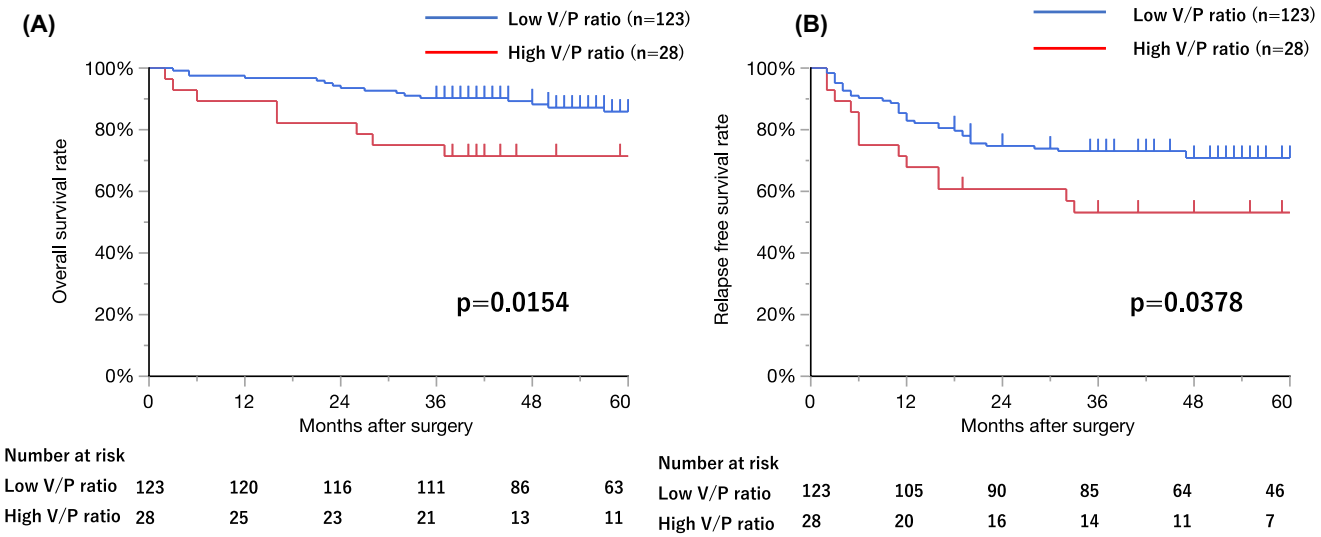

FIGURE 3 Kaplan–Meier curves for overall survival and relapse-free survival according to the V/P ratio. (A) Overall survival. (B) Relapse-free survival.

TABLE 2 Univariate and multivariate analyses for overall survival.

	Univariate		Multivariate	
Characteristics	**HR (95% CI)**	***p*-value**	**HR (95% CI)**	***p*-value**
Age, y				
65>	1	0.0901		
65≦	2.02 (0.89–4.55)			
Sex				
Female	1	0.3049		
Male	1.54 (0.67–3.55)			
BMI, kg/m^2				
21.06>	1	0.1332		
21.06≦	2.11 (0.79–5.60)			
PMI, cm^2/m^2 (men 6.36 cm^2/m^2, women 3.92 cm^2/m^2)				
High	1	0.2003		
Low	1.81 (0.72–4.53)			
Sarcopenic obesity				
Absence	1	0.4116		
Presence	1.65 (0.49–5.53)			
Diabetes mellitus				
Absence	1	0.3584		
Presence	1.53 (0.61–3.82)			
Tumor location				
Rectum	1	0.8634		
Colon	1.07 (0.49–2.31)			
Pathological stage				
I, II	1	0.4216		
III	1.41 (0.61–3.25)			
Postoperative complication (CD ≧II)				
Absence	1	0.0148	1	0.0116
Presence	2.63 (1.20–5.75)		2.73 (1.25–5.97)	
V/P ratio				
13.7>	1	0.0499	1	0.0365
13.7≦	2.30 (1.01–5.30)		2.43 (1.05–5.61)	

($p = 0.0218$) were independent poor prognostic factors for OS (Table 4).

4 | DISCUSSION

In our study a high V/P ratio was found to be an independent poor prognostic factor in patients with colorectal cancer. To our knowledge, this is the first report on the V/P ratio in colorectal cancer. In this study, a high V/P ratio was an independent poor prognostic factor even in patients who did not have obesity, as defined by the BMI. This is useful for identifying potential sarcopenic obesity in patients that cannot be determined by BMI alone.

In this study OS and RFS were significantly worse in the high V/P ratio group. A high V/P ratio indicates increased relative fat mass and decreased skeletal muscle mass, and the body composition of patients with a high V/P ratio is similar to that of patients with sarcopenic obesity. It is speculated that sarcopenic obesity causes decreased insulin sensitivity and is associated with cardiovascular disease and cancer.[24] Reduced insulin sensitivity in sarcopenic obesity increases diabetes mellitus, hypertension, hyperlipidemia, cardiovascular disease, and mortality.[7,24] Elevated insulin resistance leads to hyperinsulinemia, and elevated insulin-like growth factor 1 also contributes to poor oncologic prognosis by causing activation of tumor cell growth signals.[11,24] The high V/P ratio group was significantly more likely

TABLE 3 Patient characteristics in nonobese patients.

Characteristics	V/P ratio		
	Low ($n=102$, <13.7)	High ($n=14$, ≧13.7)	p-value
Age, y [mean (SD)]	63.7 (13.0)	68.5 (8.07)	0.1825
Sex (%)			
Female	41 (40.1)	8 (57.1)	0.2287
Male	61 (59.9)	6 (42.9)	
BMI, kg/m^2 [mean (SD)]	20.9 (2.66)	22.8 (1.86)	0.009
VFA, cm^2 [mean (SD)]	63.4 (48.1)	157.7 (42.3)	<0.0001
SFA, cm^2 [mean (SD)]	81.2 (44.1)	110.4 (29.2)	0.0182
PMA, cm^2 [mean (SD)]	12.4 (4.92)	9.87 (2.79)	0.0548
PMI, cm^2/m^2 [mean (SD)]	4.74 (1.51)	3.81 (0.91)	0.0282
Albumin, g/dL [mean (SD)]	3.78 (0.54)	3.78 (0.57)	0.9872
Postoperative complication (CD ≧II) (%)			
Presence	37 (36.3)	3 (21.4)	0.2731
Absence	65 (63.7)	11 (78.6)	
Tumor location (%)			
Colon	50 (49.0)	9 (64.3)	0.2840
Rectum	52 (51.0)	5 (35.7)	
Pathological stage (%)			
I	8 (7.8)	1 (7.1)	0.5911
II	30 (29.4)	6 (42.9)	
III	64 (62.8)	7 (50.0)	
Postoperative adjuvant chemotherapy (%)			
Presence	57 (55.9)	9 (64.2)	0.5516
Absence	45 (44.1)	5 (35.8)	
Diabetes mellitus (%)			
Presence	12 (11.8)	7 (50.0)	0.0003
Absence	90 (88.2)	7 (50.0)	

Abbreviations: BMI, body mass index; CD, Clavien–Dindo classification; PMA, psoas muscle area; PMI, psoas muscle index; SD, standard deviation; SFA, subcutaneous fat area; VFA, visceral fat area.

to have diabetes mellitus, suggesting that insulin resistance as well as sarcopenic obesity may have been associated with poor OS and RFS. There are reports of poor OS in sarcopenic obesity and poor RFS in patients with colorectal cancer and sarcopenic obesity or high visceral fat, and the present results are consistent with those reports.[12,13,19]

The most useful finding of this study was that a high V/P ratio is an independent poor prognostic factor, identifying high-risk patients even if they do not have obesity as defined by their BMI. The prevalence of obesity differs between the Western and Asian populations. The WHO obesity standard of BMI ≥30 kg/m^2 identifies 10–20% of the population in the West as obese, while it is only 2–3% in Japan.[18] Even in the cohort of patients in this study with colorectal cancer, in which obesity is considered a risk factor,[25] only a small number (2.6% [4/151]) had a BMI of ≥30 kg/m^2. Therefore, in this study obesity was defined by the criteria of the Japan Society for the Study of Obesity.[18] By assessing the V/P ratio, a wider range of high-risk patients can be identified, including those with potential sarcopenic obesity that cannot be determined by BMI alone, which may increase the opportunity for preoperative intervention in rehabilitation and nutritional therapy.

Even in the nonobese group, a high V/P was significantly more frequently associated with diabetes mellitus, suggesting a link between the aforementioned physiologic mechanisms and prognosis. In addition, in the high V/P ratio group those who were nonobese had less muscle mass, which may reflect aspects of poor oncologic prognosis due to skeletal muscle loss. With skeletal muscle loss, myokines, skeletal muscle-derived molecules, are reduced.[26] Myokines include over 600 proteins that promote tumor immunity and inhibit tumor growth and metastatic ability.[26,27] In the nonobese high V/P ratio group, in addition to the aforementioned mechanism similar to sarcopenic obesity, myokine depletion due to low skeletal muscle may contribute to poor prognosis.

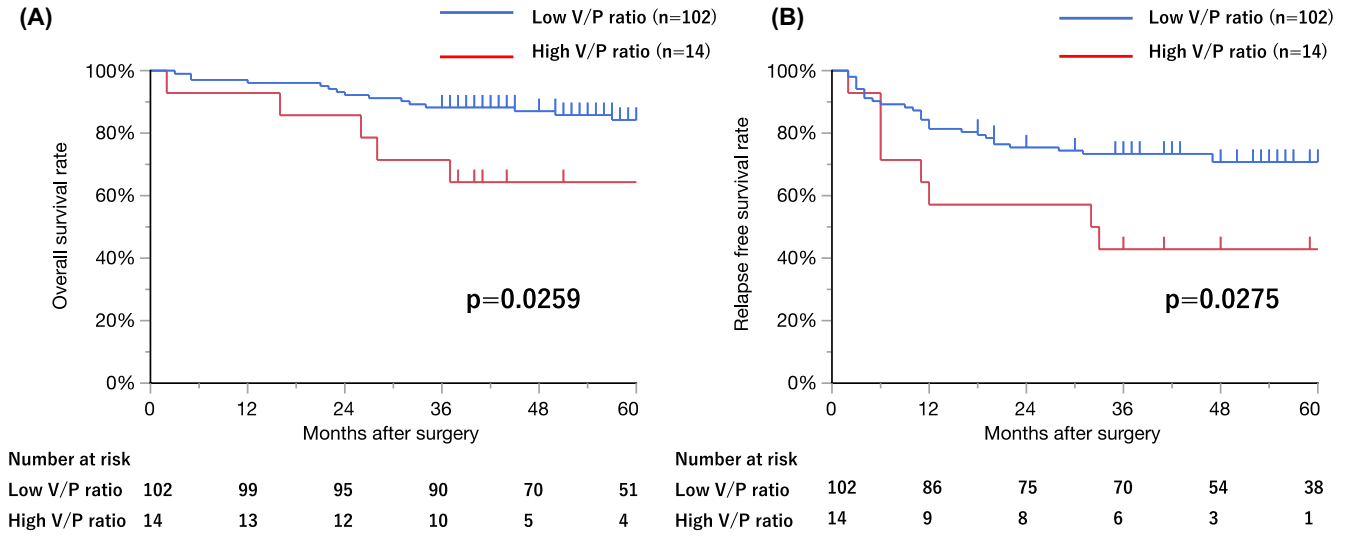

FIGURE 4 Kaplan–Meier curves for overall survival and relapse-free survival in nonobese patients according to the V/P ratio. (A) Overall survival. (B) Relapse-free survival.

TABLE 4 Univariate and multivariate analyses for overall survival in nonobese patients.

	Univariate		Multivariate	
Characteristics	**HR (95% CI)**	***p*-value**	**HR (95% CI)**	***p*-value**
Age, y				
65>	1	0.1831		
65≦	1.81 (0.75–4.38)			
Sex				
Female	1	0.1197		
Male	2.10 (0.82–5.39)			
PMI, cm^2/m^2 (men 6.36 cm^2/m^2, women 3.92 cm^2/m^2)				
High	1	0.8612		
Low	1.09 (0.40–2.96)			
Diabetes mellitus				
Absence	1	0.6738		
Presence	1.26 (0.42–3.75)			
Pathological stage				
I, II	1	0.3256		
III	1.60 (0.62–4.11)			
Postoperative complication (CD≧II)				
Absence	1	0.0315	1	0.0218
Presence	2.51 (1.08–5.82)		2.68 (1.15–6.24)	
V/P ratio				
13.7>	1	0.0446	1	0.0273
13.7≦	2.81 (1.02–7.70)		3.13 (1.13–8.63)	

The V/P ratio is convenient and simple to evaluate using CT imaging performed preoperatively. In addition, the identification of a wider range of high-risk patients, both obese and nonobese, may contribute to improving prognosis by increasing the opportunity for preoperative intervention with rehabilitation and nutritional therapy.[28] Sarcopenic obesity has been reported to have poor prognostic potential in various carcinomas such as pancreatic and liver cancer.[12,13,29,30] It may be possible to identify patients

with poor prognosis relating to a mechanism similar to sarcopenic obesity, not only for colorectal and esophageal cancer,[20] but also other carcinomas.

This study has some limitations. First, the sample size was small because this was a single-center study, and the optimal V/P ratio cutoff value was unknown. The cutoff value for OS was calculated from the ROC curve; however, owing to the small number of patients, further investigation is needed in a large multicenter study. Second, we did not adequately consider the details of adjuvant chemotherapy (for example, the type and dose of the drug and whether it was completed or not), which may impact prognosis. Further studies are needed to investigate whether adjuvant therapy affects the observed poor prognosis for patients with a high V/P ratio. Despite these limitations, the findings indicate that preoperative evaluation of the V/P ratio, which has been associated with prognosis, can help identify potential high-risk cases, even among patients without obesity, and may contribute to improved prognosis by providing opportunities for preoperative intervention and close follow-up.

In conclusion, the V/P ratio is an important prognostic indicator for colorectal cancer. It may be useful in identifying high-risk patients preoperatively, whether obese or nonobese.

AUTHOR CONTRIBUTIONS

Conceptualization, Data curation & Formal analysis: NH and TS; Investigation: NH; Methodology: NH and TS; Software: NH; Supervision, Validation & Visualization: NH; Writing – original drafts: NH and TS; Writing –review & editing: NH, TS, TO, KO, TY, MS, HO, MS, KS, and HS.

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CONFLICT OF INTEREST STATEMENT

Author Ken Shirabe is an editorial board member of the *Annals of Gastroenterological Surgery*. The other authors declare no conflicts of interest for this article.

ETHICS STATEMENT

Approval of the research protocol: The protocol for this research project has been approved by a suitably constituted Ethics Committee of the institution and it conforms to the provisions of the Declaration of Helsinki. Committee of the Graduate School of Medicine, Gunma University, Approval No. HS2023-097. Informed consent was obtained through an opt-out on the website.

Informed Consent: Informed consent was obtained through an opt-out on the website.

Registry and the Registration No. of the study/trial: Committee of the Graduate School of Medicine, Gunma University, Approval No. HS2023-097.

Animal Studies: N/A.

ORCID

Nobuhiro Hosoi https://orcid.org/0009-0005-4381-4703
Takuya Shiraishi https://orcid.org/0000-0003-3543-1874
Makoto Sakai https://orcid.org/0000-0003-0860-3132
Hiroomi Ogawa https://orcid.org/0000-0002-6416-6267
Hiroshi Saeki https://orcid.org/0000-0001-7243-6960

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