Sarcopenia and Charlson Comorbidity Index are Risk Factors for Short-Term Postoperative Prognosis of Elderly Patients with Gastrointestinal Tumor: A Retrospective Study

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Abstract

Background

Sarcopenia is one of the most common syndromes in the older adults. Gastrointestinal tumor is a malignant disease with high incidence. This study aimed to investigate the risk factors of sarcopenia in older adults with gastrointestinal tumor, the prognostic indicators of and short-term outcomes after resection for gastrointestinal tumor, and to explore the relationship between sarcopenia and short-term postoperative prognosis.

Method

A total of 247 older patients with gastrointestinal tumors who underwent radical resection in 2019 were included in this study. Relevant indexes were calculated using L3 slice image of computed tomography (CT) to evaluate sarcopenia. Short-term postoperative complications and length of stay were considered as short-term outcome of this study.

Results

Advanced age, lower higher body mass index (BMI), lower hemoglobin, having history of abdominal surgery and higher visceral fat index (VFI) were risk factors of sarcopenia, while higher BMI and lower subcutaneous fat index (SFI) were protective factors of sarcopenia. Further multivariate logistic regression analysis showed that having history of abdominal surgery, advanced age and lower BMI were independent risk factors. Sarcopenia and higher Charlson comorbidity index were independent risk factors of short-term postoperative complications in the elderly with gastrointestinal tumor. Higher Charlson comorbidity index gave rise to longer length of stay.

Conclusions

Sarcopenia and higher Charlson comorbidity index predict poor short-term prognosis of older patients undergoing gastrointestinal tumor resection.

1. Introduction

Sarcopenia is one of the most common syndromes in the older adults. As newly released guideline, sarcopenia is defined as a decline in muscle quality, strength and function which are associated with aging [1]. The prevalence of sarcopenia varies among different regions and ethnic groups [2]. With the aging tendency of global population, the number of people with sarcopenia is increasing. Patients with sarcopenia have a higher risk of falls, fractures, and motor functional decline. In recent years, more and more studies on sarcopenia have been conducted, and guidelines have been constantly updated at home and abroad to help clinical work and related scientific research. As previous research showed, nearly 1/10 older adults suffered with muscle quality decline [3], so that the society should attach more importance to sarcopenia.

Solid tumor of gastrointestinal tract is a malignant disease of high incidence. According to the GLOBOCAN 2018 data released by the World Health Organization (WHO) in 2018, colorectal cancer ranks the third and gastric cancer the fourth among the top ten tumors in terms of incidence [4]. There are about 1.4 million new cases of colorectal cancer and 1 million new cases of stomach cancer each year globally, and about 70 percent of stomach cancer occurs in developing countries [4]. In China, there are a large number of patients with colorectal cancer and stomach cancer, and the effective treatment for most of them potentially is surgical resection. Older adults with cancer have a higher incidence of sarcopenia [5]. Recent studies have shown that sarcopenia is correlated with the poor prognosis after resection surgery for colorectal cancer and stomach cancer [6, 7]. However, relevant research in the Chinese population is still limited.

Therefore, this study explored the relationship between sarcopenia, common clinical indicators and short-term postoperative complications in older patients with colorectal cancer and gastric cancer. We aimed to further identify prognostic indicators for older patients with resection and to intervene precisely.

2. Method

2.1. Patients

Older patients undergoing resection for gastric cancer or colorectal cancer at the First Affiliated Hospital of Zhejiang University from January to December in 2019 were included in this retrospective study. Inclusion criteria were: 1. patients' age ≥ 70 years old; 2. Abdominal CT were completed within 15 days before the surgery; 3. Postoperative pathology confirmed malignant tumor. Patients with incomplete important data, such as leukocyte, hemoglobin, neutrophils to lymphocytes ratio (NLR), albumin, height, weight, postoperative course record and etc., were excluded from this study.

All the data were collected by experienced geriatrician from electronic medical records, which included: basic information such as sex, height, weight, age and etc.; comorbidities were evaluated by Charlson comorbidity index [8]; history of abdominal surgery; history of alcohol, tobacco; laboratory parameters included leukocyte, hemoglobin, albumin and NLR within 15 days before the surgery; CT slice at L3; the operation data included the duration of operation, intraoperative blood loss, and postoperative pathology; cancer stage which was based on The Union for International Cancer Control (UICC) cancer tumor node metastasis (TNM) staging system (8th edition) [9]; and postoperative outcomes included postoperative complications which was evaluated by Clavien-Dindo classification [10] and length of stay.

2.2. Imaging Analysis

The CT slice at L3 was analysed by Image J (NIH Image J version 1.52a). Referred to the former research, skeletal muscle threshold is -29HU to 150HU and the adipose tissue threshold is -190HU to -30HU [6]. An example is shown in Fig. 1, in which the red part represents muscle tissue, the dark green part represents subcutaneous fat tissue, and the light green part represents visceral fat tissue. This study measured the skeletal muscle area (SMA), subcutaneous fat areas (SFA) and visceral fat area (VFA). Obtained area

values were divided by the square of the patient's height (m^2) to skeletal muscle index (SMI), SFI and VFI. Visceral-to-subcutaneous ratio of fat area (VSR) was also calculated as a parameter. According to the previous large sample Chinese population study, male $SMI \leq 40.8 \text{ cm}^2/m^2$ and female $SMI \leq 34.9 \text{ cm}^2/m^2$ were defined as sarcopenia [11].

2.3.Statistics

Data are given as means (with standard deviation) or medians (with interquartile range). Univariate and multivariate logistic regression were performed to analyse the related variables of postoperative complications. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Linear regression was performed to analyse the related factors for length of stay. IBM SPSS 25 was used for all this analysis.

3. Results

3.1. Patients characteristics

The characteristics of included patients were presented in Table 1. A total of 247 older patients undergoing gastrointestinal tumor surgery were included in this study, 163 of them were men. 98 patients were diagnosed with gastric cancer and the rest with colorectal cancer. Their average age was about 75.5 and their average BMI was around $22.2 \text{ kg}/m^2$. 52 patients had history of alcohol and 60 patients had history of tobacco and most of them were male. 60 patients had history of abdominal surgery. The mean values of leukocyte, hemoglobin, albumin and NLR were within the range of normal clinical values. Most of the patients were in TNM stage I and II, but only 13 patients were defined as well differentiated histologic type.

Using the ImageJ software, we calculated the parameters of human body composition. SMI, SFI, VFI and VSR were $45.6 \pm 9.8 \text{ cm}^2/m^2$, $32.1 \pm 18.7 \text{ cm}^2/m^2$, $49.6 \pm 42.0 \text{ cm}^2/m^2$, 1.69 ± 0.75 in men, $36.9 \pm 8.6 \text{ cm}^2/m^2$, $51.9 \pm 28.0 \text{ cm}^2/m^2$, $49.0 \pm 27.4 \text{ cm}^2/m^2$, 0.99 ± 0.42 in women.

Table 1: Overall characteristics of patients.

	Men(n=163)	Women(n=84)	Total(n=247)
Age(years)	75.34(4.70)	75.79(5.01)	75.5(4.8)
Cancer site, n(%)			
gastric	77(31.1)	21(8.5)	98(39.7)
colorectal	86(34.8)	63(25.5)	149(60.3)
BMI(kg/m ²)	22.5(3.2)	21.9(3.3)	22.2(3.2)
Charlson comorbidity index	4(1)	4(2)	4(2)
History of alcohol, n(%)	48(19.4)	4(1.6)	52(21.1)
History of tobacco, n(%)	67(27.1)	1(0.4)	68(27.5)
History of abdominal surgery, n(%)	34(13.7)	26(10.5)	60(24.3)
Major laboratory indicators			
Leukocyte($\times 10^9/L$)	5.6(2.2)	5.9(2.2)	5.7(2.1)
Hemoglobin(g/L)	131.0(31.0)	120.0(29.8)	126.5(32.0)
Albumin(g/L)	41.5(7.1)	42.7(5.6)	42.1(6.7)
NLR	2.5(1.4)	2.1(1.6)	2.4(1.5)
Intraoperative blood loss(ml)	123.4(92.8)	103.8(80.1)	116.3(89.0)
Duration of operation(min)	195(67)	174(55)	188(65)
Cancer stage, n(%)			
I	70(28.3)	28(11.3)	98(39.7)
II	57(23.1)	26(10.5)	83(33.6)
III	36(14.6)	30(12.1)	66(26.7)
Histologic type, n(%)			
Poorly differentiated	66(26.7)	33(13.4)	99(40.1)
Moderately differentiated	90(36.4)	46(18.6)	136(55.1)
Well differentiated	7(2.8)	6(2.4)	13(5.3)
Body composition			
SMI(cm ² /m ²)	45.6(9.8)	36.9(8.6)	42.6(10.9)
SFI(cm ² /m ²)	32.1(18.7)	51.9(28.0)	37.6(24.3)
VFI(cm ² /m ²)	49.6(42.0)	49.0(27.4)	49.4(35.7)

VSR	1.69(0.75)	0.99(0.42)	1.45(0.77)
Postoperative complication, n(%)	37(15.0)	28(11.3)	65(26.3)
Length of stay(day)	10(4)	9(4)	9(5)

Abbreviations: BMI= body mass index; NLR= neutrophil to lymphocyte ratio; SMI=skeletal muscle index; SFI= subcutaneous fat index; VFI= visceral fat index; VSR= visceral to subcutaneous ratio of fat area.

3.2. Factors associated with sarcopenia

71 patients were classified as sarcopenia. The incidence of sarcopenia in these patients with digestive tract tumors was about 28.7%.

This study detected several factors associated with sarcopenia as Table 2 showed. In univariate analysis, sarcopenia was associated with advanced age ($p=0.001$), lower BMI ($p=0.001$), lower hemoglobin ($p=0.009$), having history of abdominal surgery ($p=0.010$), and higher VFI ($p=0.001$). Higher BMI ($p=0.001$) and lower SFI ($p=0.005$) were protective factors for sarcopenia. Multivariate logistic regression was used to further analyse the data and it showed that having history of abdominal surgery (OR:2.5; 95% CI:1.3 to 5.3; $p=0.007$), advanced age (OR:3.0; 95% CI:1.6 to 5.7; $p=0.001$) and lower BMI (OR:3.4; 95% CI:1.3 to 8.6; $p=0.011$) were independent risk factors for sarcopenia.

Table 2: Univariate and multivariate logistic regression analysis of sarcopenia associated factors.

Variable	Univariate analysis			Multivariate analysis		
	OR	95%CI	p Value	OR	95%CI	p Value
Sexa	0.6	0.3-1.1	0.084			
Ageb	3.2	1.8-5.8	0.001	3	1.6-5.7	0.001
Cancer sitec	0.6	0.3-1.1	0.078			
BMI ^d	3.3	1.3-8.0	0.009	3.4	1.3-8.6	0.011
BMI ^{d*}	0.2	0.1-0.4	0.001	0.2	0.1-0.4	0.001
Charlson comorbidity indexe	1.5	0.8-2.7	0.207			
History of alcoholf	1.7	0.8-3.1	0.086			
History of tobacco ^g	1.5	0.8-2.8	0.252			
History of abdominal surgery ^h	2.2	1.2-4.1	0.010	2.6	1.3-5.3	0.007
Leukocytei	1.4	0.8-2.4	0.254			
Hemoglobin ^j	2.1	1.2-3.7	0.009			
Albumin ^k	1.7	0.9-2.9	0.075			
NLR ^l	0.7	0.4-1.2	0.159			
Cancer stagem	1.1	0.8-1.5	0.470			
Histologic typen	1	0.6-1.7	0.860			
SFI ^o	0.4	0.3-0.8	0.005			
VFI ^p	2.9	1.6-5.3	0.001			
VSR ^q	1.0	0.6-1.7	0.985			

a. Female as reference; b. age ≤ 75 as reference; c. colorectal cancer as reference; d. BMI $< 18.5 \text{ kg/m}^2$ vs $18.5 \text{ kg/m}^2 \leq \text{BMI} \leq 24 \text{ kg/m}^2$; d*. BMI $> 24 \text{ kg/m}^2$ vs $18.5 \text{ kg/m}^2 \leq \text{BMI} \leq 24 \text{ kg/m}^2$; e. Charlson comorbidity index ≤ 4 as reference; f. no history of alcohol as reference; g. no history of tobacco as reference; h. no history of abdominal surgery as reference; i. leukocyte ≥ 5.7 as reference; j. hemoglobin ≥ 126.5 as reference; k. albumin ≥ 42.1 as reference; l. NLR ≥ 2.4 as reference; m. stage I and stage II vs stage III; n. moderately and well differentiated vs poorly differentiated; o. SFI $\leq 37.6 \text{ cm}^2/\text{m}^2$ as reference; p. VFI $\leq 49.4 \text{ cm}^2/\text{m}^2$ as reference; q. VSR ≤ 1.45 as reference.

Abbreviations: OR= odds ratio; CI= confidence interval; BMI= body mass index; NLR= neutrophil to lymphocyte ratio; SMI=skeletal muscle index; SFI= subcutaneous fat index; VFI= visceral fat index; VSR= visceral to subcutaneous ratio of fat area.

3.3. Relationship between sarcopenia and postoperative complication

About 62 patients had grade two and above of Clavien-Dindo classification of surgical complications. The main complications included postoperative hemorrhage, pulmonary infection, abdominal infection, seroperitoneum, delirium, anastomotic leakage, ileus, venous thrombosis, heart failure, etc. Exploratory laparotomy was performed in four patients after operation because of the postoperative hemorrhage or ileus. One patient got interventional operation for multiple thrombosis. 1 patient died because of hemorrhoea. One patient discharged from hospital giving up treatment because of severe infection and bone marrow suppression.

Several factors were found associated with postoperative complications as Table 3 presented. In univariate analysis, advanced age ($p=0.012$), higher Charlson comorbidity index ($p=0.014$), and sarcopenia ($p=0.001$) were associated with postoperative complications. Further multivariate logistic regression analysis showed that sarcopenia (OR:2.6; 95% CI:1.4 to 4.9; $p=0.002$), and higher Charlson comorbidity index (OR:2.1; 95% CI:1.1 to 3.9; $p=0.026$) were independent risk factors of postoperative complications.

Table 3: Univariate and multivariate logistic regression analysis of postoperative complications associated factors.

Variable	Univariate analysis			Multivariate analysis		
	OR	95%CI	p Value	OR	95%CI	p Value
Sexa	1.4	0.8-2.6	0.226			
Ageb	2.1	1.2-3.8	0.012			
Cancer sitec	1.7	0.9-3.1	0.095			
BMI ^d	2.2	0.9-5.4	0.097			
BMI ^{d*}	0.8	0.4-1.6	0.618			
Charlson comorbidity indexe	2.2	1.2-4.0	0.014	2.1	1.1-3.9	0.026
History of alcohol ^f	2.2	0.9-4.9	0.067			
History of tobacco ^g	1.1	0.6-2.1	0.723			
History of abdominal surgery ^h	1.8	1.0-3.5	0.065			
Leukocytei	1.3	0.7-2.3	0.400			
Hemoglobin ^j	1.2	0.7-2.1	0.207			
Albumin ^k	0.9	0.5-1.7	0.851			
NLR ^l	0.7	0.4-1.2	0.207			
Cancer stage ^m	1.8	1.0-3.3	0.060			
Histologic type ⁿ	1.2	0.7-1.9	0.510			
Sarcopenia ^o	2.7	1.5-5.0	0.001	2.6	1.4-4.9	0.002
SF ^p	0.8	0.5-1.4	0.442			
VFI ^q	0.9	0.5-1.6	0.696			
VSR ^r	1.4	0.8-2.4	0.288			
Intraoperative blood loss ^s	1.4	0.7-2.6	0.386			
Duration of operation ^t	1.8	1.0-3.2	0.051			

a. Female as reference; b. age ≤ 75 as reference; c. colorectal cancer as reference; d. BMI $\geq 18.5 \text{ kg/m}^2$ vs $18.5 \text{ kg/m}^2 \leq \text{BMI} \leq 24 \text{ kg/m}^2$; d*. BMI $\geq 24 \text{ kg/m}^2$ vs $18.5 \text{ kg/m}^2 \leq \text{BMI} \leq 24 \text{ kg/m}^2$; e. Charlson comorbidity index ≤ 4 as reference; f. no history of alcohol as reference; g. no history of tobacco as reference; h. no history of abdominal surgery as reference; i. leukocyte ≥ 5.7 as reference; j. hemoglobin ≥ 126.5 as reference; k. albumin ≥ 42.1 as reference; l. NLR ≥ 2.4 as reference; m. stage I and stage II vs stage III; n. moderately and well differentiated vs poorly differentiated; o. without sarcopenia as reference; p.

SFI $\leq$ 37.6cm²/m² as reference; q. VFI $\leq$ 49.4cm²/m² as reference; r. VSR $\leq$ 1.45 as reference; s. blood loss $\leq$ 116ml as reference ; t. time $\leq$ 196min as reference.

Abbreviation:OR= odds ratio; CI= confidence interval; BMI= body mass index; NLR= neutrophil to lymphocyte ratio; SMI=skeletal muscle index; SFI= subcutaneous fat index; VFI= visceral fat index; VSR= visceral to subcutaneous ratio of fat area.

3.4. Factors associated with length of stay

Linear regression was used to analyze the risk factors associated with length of stay. After the factors which were correlated with each other were excluded, it was found that Charlson comorbidity index ($p=0.019$), tumor site ($p=0.016$), and duration of surgery ($p=0.045$) were significantly correlated with length of hospital stay. Higher Charlson comorbidity index and longer operative time will result in longer hospital stays. The length of stay of patient with gastric cancer was significantly longer than those who with colorectal cancer.

4. Discussion

This study mainly investigated the risk factors of sarcopenia in older patients with digestive tract tumors and the relationship between sarcopenia and short-term postoperative outcome. This study found that the incidence of sarcopenia in older patients with gastric cancer or colorectal cancer was about 28.7%, which was clearly associated with history of abdominal surgery, lower BMI, and advanced age. The occurrence of postoperative complications was correlated with sarcopenia and higher Charlson comorbidity index.

The Asian Working Group for Sarcopenia (AWGS) released the latest expert consensus on the diagnosis and treatment of sarcopenia in 2019. Sarcopenia is defined as age-related loss of muscle mass accompanied by a decline in muscle strength and function which is the same as 2014 edition [1]. The commonly used methods for muscle mass measurement are DXA or BIA, and CT is also recognized as a good method for skeletal muscle mass measurement especially for assessing muscle volume [12]. However, there is some debates on the diagnostic threshold. In general studies, L3 plane was selected to calculate the muscle area and SMI value. Sarcopenia was defined by the cut-off value of SMI. A study published in The Lancet Oncology in 2008 suggested that men with SMI < 52.4 cm²/m² and women with SMI < 38.5 cm²/m² were considered to have sarcopenia [13]. This cut-off value is frequently used. Different ethnic groups suit different SMI cut-off value and some studies chose more complicated cut-off values according to both BMI value and SMI value [14]. Since the object of this study was Asian population, and there is a big difference in physique between the western population and Asian population, we referred to a dependable study of a large sample of Chinese population in which men with SMI $\leq$ 40.8 cm²/m² and women with SMI $\leq$ 34.9 cm²/m² were considered to have sarcopenia [11]. The

prevalence of low muscle mass in older adults with cancer was higher than in which without cancer according to previous researches [15]. In this study, 71 patients (28.7%) were considered with sarcopenia.

Whether sarcopenia is a risk factor of short-term postoperative complications in older patients is still controversial. Some studies showed that the surgical complications of patients with oesophageal cancer had no relation with sarcopenia [16], while in some other cancer such as lung cancer and renal cell carcinoma, sarcopenia seemed to be related with prognosis of surgery [17][18]. This study suggested that sarcopenia was a dependent risk factor of short-term postoperative complications in older patients with gastric cancer or colorectal cancer, and confirmed that sarcopenia is an important indicator of postoperative prognosis which suggests the necessity of preoperative diagnosis of sarcopenia. This research did not show any relationship between tumor stage, histologic type and surgical prognosis. A larger sample size may be needed for further clarification. In the univariate logistic regression analysis, this research also showed that advanced age and higher Charlson comorbidity index were risk factors for short-term surgical complications. Age was excluded in the multivariate logistic regression analysis because of the clear association between age and sarcopenia. A previous study showed that Charlson comorbidity index is an independent risk factor of short- and long-term mortality in hospitalized elderly patients and another one suggested that higher Charlson comorbidity index is related with postoperative complication and longer length of stay in patients with colorectal carcinoma [19]. This study was consistent with the previous research results. Sarcopenia was not found associated with the length of stay, while higher Charlson comorbidity index was a risk factor for longer length of stay, suggesting that patients with more underlying diseases should be taken better postoperative care.

Among the several factors related to sarcopenia found in this study, lower BMI and advanced age have been well discussed and recognized in previous studies [20]. But this research also found that higher BMI was a protective factor for sarcopenia, which may be somewhat controversial. Recently, many studies believed that obesity is also a risk factor for sarcopenia, and obesity sarcopenia became a hot research topic [1]. However, there also have been many papers suggesting that obesity is not associated with sarcopenia [21], and obesity sarcopenia was not made a clear definition and diagnosis in the newly released sarcopenia guideline [1]. This study found that higher VFI is a risk factor for sarcopenia, while higher SFI is a protective factor for sarcopenia, that is, fat in different parts of the body has different effects on sarcopenia. Some research suggested that abdominal obesity is associated with the development of sarcopenia and parameter VSR is used as a parameter to define abdominal obesity [22]. VSR reflects differences in fat distribution, but cannot reflect the volume of fat. This study did not find any correlation between VSR and sarcopenia or postoperative outcomes. The value of VSR in sarcopenia needs further research efforts. The relationship between obesity and sarcopenia is still controversial and the mechanism is still unknown, which needs to be clarified by further studies. This study also found that the occurrence of sarcopenia was associated with a prior history of abdominal surgery which was not often mentioned in other studies. Abdominal surgery may lead to the functional decline of digestive system and results in emaciation.

This study was a retrospective study, and had some limitations. There was no follow-up of the long-term prognosis of the patients, such as long-term complications and quality of postoperative life. Due to the incompleteness of preoperative surgical examination, some possible relevant nutritional indicators, such as prealbumin, were not included in this study. Our team will continue investigating the subject.

5. Conclusions

Age, lower BMI, and history of abdominal surgery are independent risk factors of sarcopenia in the older patients with gastrointestinal tumor. Sarcopenia and Charlson comorbidity index can predict the short-term prognosis of older patients undergoing gastrointestinal tumor resection.

Abbreviations

computed tomography, CT; body mass index, BMI; visceral fat index, VFI; subcutaneous fat index, SFI; World Health Organization, WHO; neutrophils to lymphocytes ratio, NLR; Union for International Cancer Control, UICC; tumor node metastasis, TNM; skeletal muscle area, SMA; subcutaneous fat area, SFA; visceral fat area, VFA; skeletal muscle index, SMI; Visceral-to-subcutaneous ratio of fat area, VSR; odds ratio, OR; confidence interval, CI; Asian Working Group for Sarcopenia, AWGS.

Declarations

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Authors' contribution

J W: project development, data analysis, manuscript writing. L X: project development, data analysis. S H: data analysis, manuscript editing. Q H: data collection. X S: data collection. Q Z: project development, manuscript editing. All authors have read and approved this manuscript.

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Ethic approval

The study protocol has got written approval of the Ethics Committee of the first affiliated hospital of Zhejiang university school of medicine.

Consent for publication

Not applicable.

Availability of data and material

The data in this study is not publicly available since national juridical restrictions, but further description or analysis of data are available from authors with reasonable request.

Competing interests

The authors declare that they have no conflicts of interest to this work.

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Figures

Figure 1

skeletal muscle and fat tissue in L3