ORIGINAL ARTICLE

# Relationship between Sarcopenia in Abdomen CT Scan Results with C-Reactive Protein Level in Colorectal Cancer Patients at Dr. Soetomo General Academic Hospital Surabaya

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**ABSTRACT**

**Introduction:** Colorectal cancer is the third most malignant and the fourth largest cause of death in the world, one of which is caused by cachexia cancer. Sarcopenia is the main diagnostic criterion for cachexia. The inflammatory response, one of the markers of which is C-Reactive Protein (CRP), is also involved in the occurrence of sarcopenia associated with cachexia cancer. This study was aimed to determine the occurrence of sarcopenia and its relationship with CRP preoperative colorectal cancer patients.
**Methods:** This type of observational retrospective analytic study assessed sarcopenia based on the Psoas muscle index (IOP) on preoperative CT scan images and CRP levels measured by an integrated automatic tool Dimension RxL Max with Flex liquid reagent preoperative CRP range (RCRP).
**Results:** Sarcopenia occurs in male colorectal cancer patients with a p-value of 0.001<0.05 (5%) with an IOP mean value of 26.75 m2, while in female patients the IOP mean value was 21.33 m2, it does not occur sarcopenia with p-value 0.583>0.05 (5%). There was an increase in CRP in 62.5% of colorectal cancer patients, but the relationship between IOP values and CRP values of colorectal cancer patients was still categorized as weak with p value of -0.387 in men and -0.046 in women with α=0.05.
**Conclusion:** There was a nonsignificant relationship between sarcopenia and CRP levels in colorectal cancer patients. Further prospective studies are required to consider the indicators of sarcopenia besides the decrease in IOP and identification of confounding factors known to be associated with CRP, muscle strength, and muscle mass.

## Introduction

The incidence of colorectal cancer reached 1.4 million new cases in 2012 with a mortality rate of 700,000 people worldwide.[1] In Indonesia there are no colorectal cancer incidence and mortality rates, and most sufferers come in an advanced stage, so their life expectancy is low. Most patients with advanced cancer experience weight loss and the main cause is cachexia cancer.[9]
The international consensus establishes sarcopenia, the main diagnostic criterion for cachexia.[2,3] Sarcopenia or a decrease in skeletal muscle mass is a problem that often occurs in cancer patients who have either experienced therapy or have not experienced therapy, and have a negative impact on physical function and quality of life. This condition is currently gaining special attention in the literature on cancer because sarcopenia can predict poor post-operative outcomes and increase postoperative morbidity and mortality and other adjuvant therapies.[4,5]

A single skeletal muscle examination to establish a diagnosis of decreased muscle mass is now a trend in many of the literature related to examination using imaging.[6] One of the single skeletal muscle that is often used to measure muscle mass loss is psoas. The selection of the psoas muscle as a sentinel muscle to determine the decrease in muscle mass is more due to the reason for ease of measurement and the accuracy of the dimensions of the imaging examination.[7] In addition to being used for evaluating nutritional status, the psoas muscle is also used to predict patient prognosis

and toxicity evaluation of chemotherapy for cancer patients.[6]

Accurate measurement of anatomic and fat-free skeletal muscles is obtained by two imaging techniques, namely computerized tomography (CT) and magnetic resonance imaging (MRI).[8] In this study, a screening method using CT scans was used because MRI examination was very expensive, not easily accessible, and not routinely done in patients with colorectal cancer cases. MRI readings also require highly specialized staff, special software, and relatively long inspection times. Patient-based studies show an inflammatory response involved in reducing muscle mass associated with cachexia cancer.[9] One of the inflammatory markers associated with sarcopenia is C-reactive protein. It is a plasma protein that increases during systemic inflammation and one of the most commonly used inflammatory markers. The price of CRP examinations is quite affordable and the examination is easy to find.[10] Measuring CRP provides an overview of inflammatory status in the body and very important for diagnosing and monitoring many chronic health conditions.[11]

The purpose of this study was to determine the occurrence of sarcopenia and its relationship with CRP preoperative colorectal cancer patients. Cachexia cancer syndrome, which in this study was assessed based on sarcopenia, is the cause of death in about 30% - 50% of all patients with cancer,[12] so that identification of patients at risk for complications from sarcopenia allows the clinicians to make appropriate interventions.

## Methods

An observational restrospective study of patients suffering from Stage I - III Colorectal Cancer who were treated from 2016 to 2017 at Dr.Soetomo General Hospital Surabaya. We studied colorectal patients who had a pre-operative CT scan and had pre-operative CRP level checked at Dr.Soetomo General Hospital Surabaya. Patients with a history of diabetes mellitus and incomplete data were excluded from this study. This study obtained data on age, sex, height/weight, date of operation, date of discharge, pre-operative CT-Scan, and medical record.

In Indonesia, there is no psoas mass index (IOP) criteria called sarcopenia, so that before this study was carried out, preliminary study was carried out. Obtained normal IOP cut-off results in men of 32 $cm^2/m^2$ and in women of 21 $cm^2/m^2$, then IOP below the cut-off value is called sarcopenia.

Preoperative abdominal CT-scan data were collected, then measured the preoperative psoas muscle index. Examination using a CT scan machine 16 slice with Hitachi brand type ECLOS Q1E-BW1545-1 and Siemens SOMATOM Emotion 80476. The levels of preoperative C-Reactive Protein were examined using the Dimension RXL Max machine through medical records.

After collecting data and measurements, the relationship between IOP and preoperative CRP level, Body Mass Index (BMI), and Length of Stay (LoS) were analyzed using IBM SPSS statistic 24.0 (IBM Corporation, Armonk, NY, USA). P-values <0.05 were considered statistically significant. The relationship between IOP and preoperative CRP level, BMI, and LoS were analyzed using Spearman's rank correlation.

This research has been submitted to the ethics commission of the Dr.Soetomo General Hospital Surabaya before conducting research. Identity data from the results of examination of patients related to this study are kept confidential. The Ethic Committee approved this study with ethical clearance number 1077/KEPK/2019.

## Results

After applying both the inclusion and exclusion criteria, a total 40 patients were included in the analysis. The general profile of those 40 patients based on sex, age, height, weight, and BMI are noted in Table 1. Based on gender, this study consists of 21 males (52.5%) and 19 females (47.5%). The youngest patient was 17 years and the oldest was 77 years old. The results showed that the majority of colorectal cancer patients were in the age group of 41-60 years as many as 21 people (52.5%). The mean of body weight and height were at 54.20 kg±7.99 and 159.9 cm±5.69. The mean of BMI was 21.20 kg/m2±2.99 which showed that the BMI values of sample patients were mostly in the normal category.

Clinical examination results of colorectal cancer patients based on preoperative CT scans are known to have an IOP mean of 24.18±5.37. The minimum IOP value was 15.70 and the largest was 41.10. Referring to the IOP values measured by colorectal cancer patients who experienced sarcopenia were 26 people (65%) and those who did not experience sarcopenia were 14 people (35%).

The results of other clinical features in the form of CRP values from 40 preoperative colorectal cancer patients obtained an average value of 37.32 mg/L±52.82. Based on these results the range of CRP values of preoperative colorectal cancer patients has a very large diversity where the smallest CRP value was 0.2 mg/L while the largest value was 199.4 mg/L. The number of normal CRP values were in 15 patients (37.5%) and CRP values increased in 25 patients (62.5%). The mean of LOS was 8.33 days± 2,37. Most of patients were treated for 8-14 days.

The relationship between IOP and CRP values in male and female colorectal cancer patients obtained p-value, which was 0.083 and 0.853> 0.05 (5%), respectively. concluded that there was no correlation between IOP values and CRP values in colorectal cancer patients. Although both men and women show reverse tendency between IOP value and CRP value r =-0,387 and -0,046, respectively.

Furthermore, There was no correlation between IOP values and BMI values in colorectal cancer patients. The relationship between IOP and BMI values in male and female colorectal cancer patients were obtained coefficient r values of -0.262 and 0.077. In line with the relationship between IOP and BMI values, there was no significant correlation between IOP values and LoS values in colorectal cancer patients. If LoS is divided into several groups with a range of 1 week, the LoS distribution of colorectal cancer patients is mostly treated for 8-14 days (+2 weeks), which is 27 people (67.5%).

## Discussion

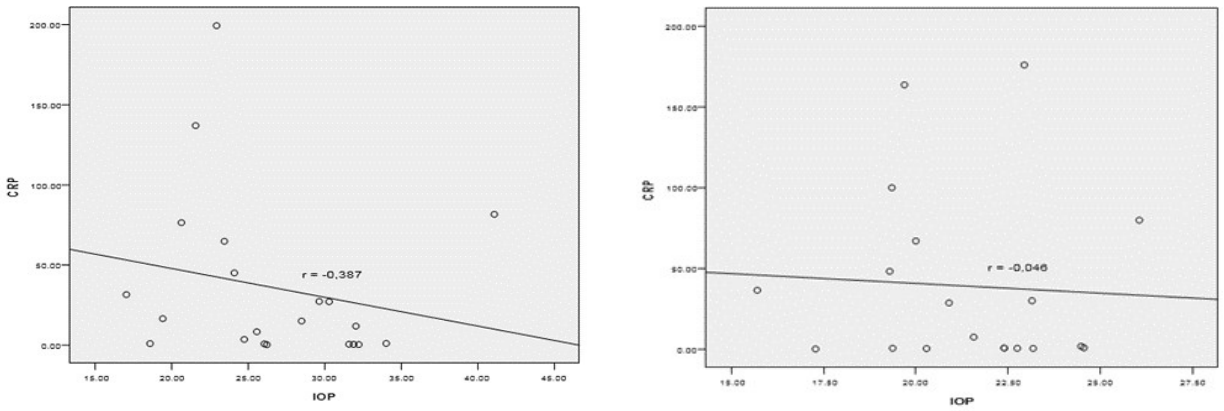
Study that correlates CRP with sarcopenia in patients with colorectal cancer has never been done. Colorectal cancer patients in Dr. Soetomo Surabaya General Hospital experience sarcopenia based on the

Table 1. General profile of patients with colorectal cancer

| Variable | Median | Mean ± SD | Range | Frequency (%) |
|---|---|---|---|---|
| Sex | | | | 21 (52.50%) |
| Male | | | | 19 (47.50%) |
| Female | | | | |
| Age (Years old) | 51.00 | 49.28 ± 13.54 | (17 - 77) | |
| Weight (kg) | 53.50 | 54.20 ± 7.99 | (40 - 76) | |
| Height (cm) | 160.00 | 159.90 ± 5.69 | (150 - 172) | |
| BMI (kg/m2) | 20.70 | 21.20 ± 2.99 | (15.6 – 28.1) | |
| Underweight | | | | 6 (15.00%) |
| Normal | | | | 29 (72.50%) |
| Overweight | | | | 5 (12.50%) |

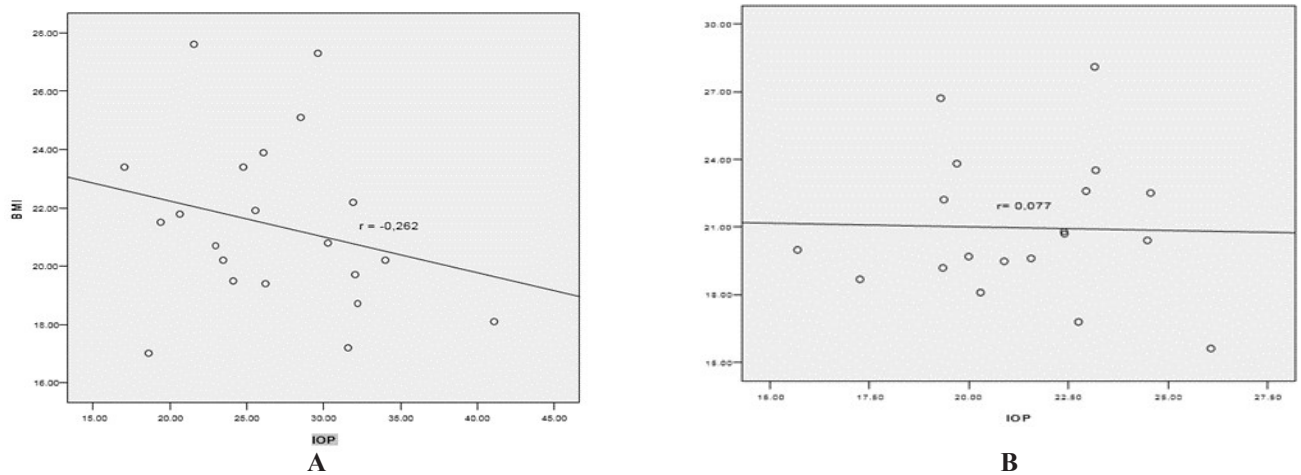
Table 2. Clinical examination results

| Variable | Median | Mean ± SD | Range | Frequency (%) |
|---|---|---|---|---|
| IOP | 23.00 | 24.18 ± 5.370 | (15.70 – 41.10) | |
| Sarcopenia (male) | | | | 81.00% |
| Sarcopenia (female) | | | | 47.40% |
| CRP | 13.40 | 37.32 ± 52.82 | (0.20 – 199.40) | |
| LOS | 8.00 | 8.33 ±2.370 | (3.00– 17.00) | |




A B

Figure 1. Relationship between IOP and CRP values in male (A) and female (B) cololacteral cancer patients using Spearman's correlation




A B

Figure 2. Relationship between IOP and BMI values in male (A) and female (B) cololacteral cancer patients using Spearman's correlation

measurement of the index of the major psoas muscle in the abdominal CT scan. We found there was no correlation between sarcopenia based on the index of the major psoas muscles with preoperative CRP levels in colorectal cancer patients. Although our result indicated reverse trend between IOP value and CRP value. If the value of IOP is getting lower then the CRP value in colorectal cancer patients will tend to be greater.

The results of the general profile of 40 colorectal cancer patients who were sampled by sex were known to patients with male sex as many as 21 patients (52.5%) while female patients were 19 patients (47.5%) (Table 1). There is no significant difference in the number of male and female sufferers. These results are consistent with data in the United States and around the world, where the incidence of colorectal cancer in men and women is the same. The role of gender in the development of colorectal cancer remains unclear. There is no data that shows the dominance of certain gender in colorectal cancer patients.[13]

Referring to the IOP values measured, colorectal cancer patients with sarcopenia were 17 people (81%) for male patients and 9 people (47.4%) in female patients with a total of 26 patients with sarcopenia (65 %). Sarcopenia occurs significantly in men compared to women.[14,15]

This shows that sarcopenia does occur in patients with colorectal cancer in RS. Dr. Soetomo Surabaya, according to previous research, among others, by Choi et al.,2017 with the results of 39.4%,[16] and by Lieffers et al.,2012 with a result of 38.9%.[17] In the previous study, the criteria for sarcopenia were not only based on a decrease in muscle mass, but combined with muscle function, so the prevalence of sarcopenia was not more than 50%.[5]

While we found inverse tendency between IOP value and CRP value, this is in line with a study by Santos et al stated that there was a positive but weak correlation between Muscle Mass and CRP in elderly patients ($r=0.27$, $p<0.01$). Their group had sample of 95 person which became a higher point than our smaller subjects number.

Potential confounders that might cause differences in results include age, gender, nutritional intake, body mass index or total body fat, smoking, alcohol use, physical activity, use of anti-inflammatory drugs, some chronic diseases, infectious diseases and metabolic diseases, cognitive, and depressive symptoms. These confounders are known to be associated with IL-6 levels, CRP, as well as muscle strength and muscle mass.[3,18]

There was no significant correlation between IOP values and BMI values in colorectal cancer patients. The results of this study are in accordance with the study where the overall prevalence of severe muscle thinning (sarcopenia) was 46.8% and was present in patients in all categories of BMI. The proportion of men who meet the criteria for sarcopenia is much higher (61%) than women (31%).[19]

The distribution of LoS for colorectal cancer patients was treated for the most 8-14 days (+ 2 weeks), which was 27 people (67.5%). This corresponds to the average hospital stay (LoS) after colectomy, which is 7 days to 10 days in the United States and more than 10 days in the UK, France, Germany, Italy and Spain.[20]

There was no correlation between IOP values and LoS values in colorectal cancer patients. These results are in line with the study by Jones et al. (2015) which stated that there was no significant difference in the overall length of stay between patients with sarcopenia and non-sarcopenia (6.23 days vs. 7.69 days $p=0.52$) and also there is no sarcopenia associated with an increase in the interval for initial mobilization.[8]

Our study has some limitations. First, it uses retrospective data to cause a limited number of samples and the possibility of sample bias. Second, in this study only consider IOP reduction when defining sarcopenia without regard to muscle function by evaluating gait speed at habitual pace over short distance and muscle strength using hand held dynamometers. Third, there is no further identification of confounding factors including nutritional intake, total body fat, smoking, alcohol use, physical activity, use of anti-inflammatory drugs, several chronic diseases, infectious diseases and metabolic diseases, cognitive disorders, and symptoms depression which is known to be associated with CRP, muscle strength and muscle mass.

## Conclusion

We found sarcopenia in colorectal cancer patients in General hospital Dr. Soetomo General Academic Hospital Surabaya based on the measurement of the index of the major psoas muscle in the CT scan of the abdomen. Also there was a weak association between sarcopenia based on the index of the major psoas muscle with levels of C-Reactive Protein preoperatively in colorectal cancer patients at General hospital Dr. Soetomo General Academic Hospital Surabaya.

## Acknowledgement

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## Conflict of Interest

Authors stated there is no conflict of interest.

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