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AGREEMENT BETWEEN SARCOPENIA SCREENING TOOLS IN COLORECTAL CANCER PATIENTS UNDERGOING CHEMOTHERAPY

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Abstract

Introduction Evidently, colorectal cancer and chemotherapy increase the risk of Sarcopenia. Therefore, sarcopenia screening is vital to prevent the adverse effect of Sarcopenia. However, there is a lack of studies regarding sarcopenia screening tools in the colorectal patient in Indonesia. Therefore, this study's objective was to determine the proportion of patients at sarcopenia risk utilizing different screening tools and agreement between those screening tools in patients with colorectal cancer undergoing chemotherapy.

Method A cross-sectional study of adult patients with colorectal cancer receiving IV chemotherapy at Kariadi General Hospital, Indonesia, was conducted. Risk of Sarcopenia utilized screening tools SARC-F, SARC-Calf (33 and 34) and SARC-Calf 31. The Kappa coefficient was calculated to identify agreement between the three tools.

Result This study included 89 colorectal patients undergoing chemotherapy, 53.9 % were male, and 82 % were malnourished. The prevalence of sarcopenia risk using SARC-F, SARC-Calf 31 and SARC-Calf (33 and 34) were 15.7 %, 29.2 % and 40.4 %, respectively. The agreement between SARC-F and SARC-Calf 31, SARC-Calf 33 and 34 was 'Fair', with k=0.3 and 0.29, respectively. SARC-Calf 31 and SARC-Calf had a substantial agreement (k=0.64)

Conclusion There was a high proportion of patients at risk of Sarcopenia using different screening tools. However, there was a variation between the proportion of sarcopenia risk and agreement between the three screening tools. Thus, further validation of sarcopenia risk screening tools for colorectal cancer patients in Indonesia is vital.

Keywords*: Sarcopenia risk, Colorectal Cancer, Chemotherapy*

INTRODUCTION

Cancer is still a leading cause of death and affects a person's quality of life worldwide. The increase in the new incidence of cancer in developing countries contributes to almost 70% of mortality-related cancer. (Gebremedhin, Cherie, Tolera, Atinafu, & Demelew, 2021) Colorectal cancer, described as a type of malignancy that occurs in the colon and or rectum, was the 3rd most new incidence and the second most mortality cases compared to other cancers worldwide, by 10 % and 9.4 %, respectively. (Sung et al., 2021) Colorectal cancer was also the fourth leading cause of death and new incidence among all cancer diagnosis in Indonesia by around 9 % in 2018. (Sung et al., 2021)

Declined muscle mass is one of the issues that colorectal cancer patients may face. This diminished muscle mass is part of the sarcopenia diagnosis component, in addition to low muscle strength and/or low physical performance based on the Asian Working Group of Sarcopenia (AWGS). (Chen et al., 2020) Sarcopenia in the cancer population is known as secondary Sarcopenia, alongside primary Sarcopenia is well known for influencing the elderly. The prevalence of Sarcopenia in the mixed cancer population ranges from 24-41 % depending on cancer site, cancer grade, assessment tools utilized and other factors. (Baracos, 2018)

Based on The Clinical Oncology Society of Australia (COSA), colorectal cancer patients are at high risk of malnutrition and Sarcopenia. (COSA, 2020) Sarcopenia in cancer patients has a negative effect on the patients, such as an increase in morbidity, mortality and a decrease in quality of life. Furthermore, during chemotherapy, Sarcopenia may increase the toxicity of chemotherapy, eventually delaying the therapy. (Marhold, Topakian, & Unseld, 2021) Moreover, Sarcopenia is related to decreased gastrointestinal cancer survival and increased morbidity in pots-surgical colorectal cancer patients. (Vergara-Fernandez, Trejo-Avila, & Salgado-Nesme, 2020)

Identification of Sarcopenia, described as recognizing patients with risk or not at risk of Sarcopenia, should be implemented for all patients at diagnosis and each therapy. Patients identified as at-risk should obtain a referral to a dietitian and exercise specialist to obtain sarcopenia assessment and suitable therapy. Several screening tools for Sarcopenia are available, for example, SARC-F and SARC-F in combination with calf-circumference, known as SARC-Calf. (COSA, 2020) Regardless of the importance of preventing Sarcopenia in this population, there is no study regarding sarcopenia risk in this population in

Indonesia. Therefore, the purpose of this study is to identify the agreement between sarcopenia risk and to describe the proportion of patients ' at risk' of Sarcopenia in this population with different screening tools.

METHODS

This study was an observational study with a cross-sectional design carried out at Kariadi General Hospital, Semarang, Indonesia, from March to April 2022. Patients aged 19 years or older undergoing intravenous chemotherapy in *Kasuari* ward, 4th and 5th floor, with a confirmed colorectal cancer diagnosis in Kariadi General Hospital, Semarang, were recruited as subjects and assessed within the first 24 hours of admission. This study is a part of the study with the title "*Malnutrition as an Associated Factor of the Sarcopenia Risk Using SARC-Calf and SARC-Calf 31 but not SARC-F in Oncology Patients Undergoing Chemotherapy*" and was approved by the ethical Committee of Kariadi General Hospital (No. 984/EC/KEPK-RSDK/2021). Characteristics of subjects, such as age, gender, type of chemotherapy, medical history, height, and past weight, were obtained through electronic patient medical records.

Nutrition status was assessed by the Patient-Generated Subjective Global Assessment (PG-SGA). PG-SGA has two parts. The patients completed the first part and were checked by a dietitian to ensure the correct answer. The first part of PG-SGA consists of evaluating weight loss percentage, nutrient intake, nutrition impact symptoms and functional capacity or activity. The second part was assessed by trained dietitians, which evaluated the metabolic stress, diseases that increase metabolic requirements (cancer, pulmonary or cardiac cachexia, age over 65 and others, and physical examination). Nutritional status is categorized as well-nourished (PG-SGA A), moderate or suspected malnutrition (PG-SGA B) and severely malnourished (PG-SGA C) based on worksheet five of PG-SGA.(Susetyowati, Yenita, & Kurnianda, 2010) Screening of Sarcopenia utilized SARC-F, SARC-Calf 31 and SARC-Calf screening tools. The SARC-F questionnaire comprises five questions regarding strength, walking ability, sitting capacity, climbing ability and number of falls. If the total score is ≥ 4, then it is categorized as having the risk of Sarcopenia. (Williams, Al-Obaidi, Dai, Bhatia, & Giri, 2021) The SARC-Calf consists of 5 questions from the SARC-F plus a calf circumference measurement. The cut-off points of Calf Circumference (CC) used in the SARC-Calf was a value under 34 cm for men and 33 cm for women, while SARC-Calf 31 of CC value was below 31 cm for both genders. The total score

on the SARC-Calf will be categorized as at risk of Sarcopenia if it shows a value of ≥11. (Souza et al., 2020) The Kappa coefficient was calculated to identify agreement between the three tools.

RESULTS

Characteristic of subjects

Participants included 89 adult patients; the majority were adults between 50-59 years old (32.6 %) and male (53.9 %), as shown in table 1. About 82 % of participants were categorized as malnourished based on PG-SGA B and C. Regarding physical activity, 88.8 % had a low activity score based on PG-SGA. Most subjects (82 %) had a Folfox chemotherapy and had at least one Nutrition Impact Symptom (83 %).

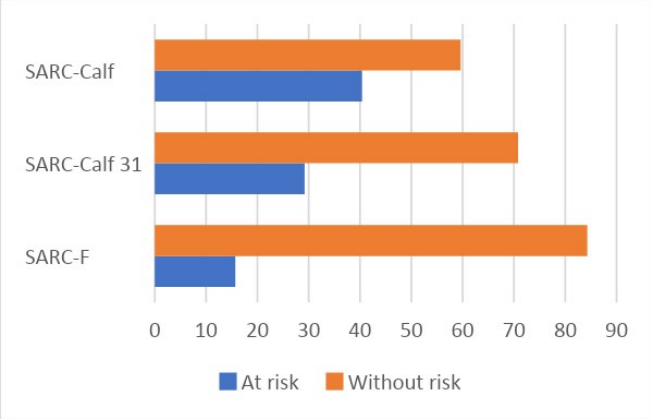
Table 1. Participant characteristics (N: 89)

Variable	n (%)
Age (years)	
19-29	4 (4.5 %)
30-39	20 (22.5 %)
40-49	28 (20.2 %)
50-59	29 (32.6 %)
>60	18 (20.2 %)
Gender	
Female	41 (46.1 %)
Male	48 (53.9 %)
Nutritional Status	
(PG-SGA)	16 (18 %)
Well-nourished (A)	61 (68.5 %)
Moderate malnutrition (B)	12 (13.5 %)
Severe Malnutrition (C)	
Activity Score (PG-SGA)	
Normal	10 (11.2 %)
Low	79 (88.8 %)
Chemotherapy drugs	
Folfox	73 (82 %)
De grammont	8 (9 %)
Folfiri	6 (6.7 %)
Other	2 (2.2 %)
Metastases	
Metastases	47 (52.8 %)
Non-metastases	42 (47.2.2 %)
Nutrition Impact	
Symptom (NIS)	14 (15.7 %)
Without NIS	75 (84.3 %)
With NIS	

The proportion of sarcopenia risk based on SARC-F, SARC-Calf 31 and SARC-Calf 33

Figure 1 pictures the proportion of participants at risk of Sarcopenia with different screening tools. Fourteen of 89 participants (15.7 %) were at risk of Sarcopenia using SARC-F screening tools, while 75 participants (84. 3 %) were not at risk utilizing the same screening tool. Sarcopenia risk was 40.4 % and 29.2 % using SARC-Calf and SARC-Calf 31, respectively.

Figure 1. comparison of sarcopenia risk prevalence utilizing SARC-Calf, SARC-Calf 31 and SARC-F



Agreement between SARC-F, SARC-Calf 31 and SARC-Calf

As described in the slide, SARC-Calf 31 and SARC-Calf 33 and 34 had a good agreement, with kappa statistics of 0.64. SARC-Calf 31 and SARC-Calf had a fair agreement, with kappa statistics of 0.30 and 0.29, respectively.

Table 2. strength of agreement between sarcopenia screening tools

Screening tools	Kappa statistics	Strength of agreement
SARC-Calf 31 and SARC-Calf	0.64[a]	Substantial Agreement
SARC-Calf 31 and SARC-F	0.30[a]	Fair Agreement
SARC-Calf and SARC-F	0.29[a]	Fair Agreement

[a] Statistically significant at 95 % CI

DISCUSSION

The prevalence of sarcopenia risk in this study ranged from 15-40 %, almost similar to the actual sarcopenia prevalence of the colorectal cancer population in the western

population (12-60 %). (Vergara-Fernandez et al., 2020) Malnutrition, physical inactivity, and age might be attributed to this high prevalence of sarcopenia risk since the proportion of participants with low activity levels, age more than 50, and malnutrition described as PG-SGA B and C, are high. Physical inactivity is common in oncology patients; chemotherapy effects, for example, fatigue, general weakness and pain, may reduce the physical activity of a person with cancer. Physical activity reduction may lead to decreased muscle strength and muscle mass, notably lower extremities. Loss of muscle mass itself can hinder the physical activity of oncology patients. (Jeffery et al., 2022; Oflazoglu et al., 2020) (Tyastuti, Suswan, & Purwaningsih, 2022) Regarding malnutrition, malnutrition in cancer patients is associated with sarcopenia risk, as a decrease in muscle mass is the component of both malnutrition and sarcopenia assessment.

Low energy intake through Nutrition Impact Symptoms (NIS) during chemotherapy may lead to Sarcopenia. NIS is any barrier that may intervene with food intake, for example, taste and smell change, nausea and vomiting, anorexia, and pain.(Omlin et al., 2013; Tyastuti, Purwaningsih, & Suswan, 2022). The frequency of two to three NIS in oncology patients was associated with poor appetite and weight loss, which may lead to malnutrition and Sarcopenia. (Omlin et al., 2013) Chemotherapy can cause mitochondrial damage and increase reactive oxygen species, which can induce oxidative muscle stress. Furthermore, chemotherapy may cause a decrease in muscle microvasculature through antiangiogenesis (Davis & Panikkar, 2019).

There is a difference in sarcopenia risk between the three tools in this study, whereas SARC-Calf 33 and 34 cm found the greater risk of Sarcopenia, followed by SARC-Calf 31. SARC-F has been validated in older people in Asia and Western countries. However, SARC-F as a screening tool for Sarcopenia is dissatisfactory in measuring muscle loss. Although this tool supports evaluating muscle function, the validity is low in screening patients at risk, particularly in the cancer population. SARC-Calf 33 and 34 have been validated to improve sarcopenia screening in the western cancer population. SARC-Calf also has been known to have the best sensitivity and specificity for the Asian elderly population. In metastatic cancer patients, SARC-Calf had better sensitivity than SARC-F, ranging from 43.3 % to 66.6 % against 15.2 %-32.1 % compared with eastern and western categories of sarcopenia diagnosis. (Fu et al., 2020)

This study concludes that there is a good agreement between SARC-Calf with different cut-off points of CC in this study. However, the cut-off points for calf

circumference in the cancer population have not been established in Indonesia. There are several studies regarding the muscle mass of the elderly in Indonesia. Pusparini found that the optimal cut-off-point for healthy elderly is 32.9 cm for females and 33.5 cm for males, while Laksmi stated that 34 cm and 29 cm for men and women are the appropriate cut-off points for elderly outpatients. (Laksmi et al., 2019; Pusparini, Probosari, Murbawani, Muis, & Christianto, 2022) Pusparini and Laksmi's studies evaluate the cut-off point of muscle mass in the elderly. To our knowledge, the cut-off point in the cancer population has not been studied yet.

The limitation of this work is that this study did not measure actual sarcopenia diagnosis. Furthermore, there was a relatively limited sample number. Further study in the future may be needed to verify this result. However, this is the first study to evaluate sarcopenia risk and agreement between sarcopenia screening tools of patients with colorectal cancer on chemotherapy in Indonesia.

CONCLUSION AND RECOMMENDATION

Depending on the tools utilized, there is a different proportion of sarcopenia risk; SARC-Calf 33 and 34 screens most cases. Ideally, as international guidelines, sarcopenia screening should be incorporated into the standard care of patients with cancer. However, this practice is uncommon in Indonesia. Sarcopenia screening is quick and easy. However, validating the suitable screening tools used in the Indonesian population is needed.

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