The relationship between IL-6 and CRP with Sarcopenia in indigenous elderly population at Pedawa Village, Buleleng, Bali, Indonesia

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Abstrak

Latar belakang: *Sarkopenia adalah sindrom yang ditandai dengan penurunan massa otot disertai penurunan kekuatan otot dan atau fungsi otot. Stres oksidatif dan proses inflamasi dikenal sebagai faktor pemicu untuk sarkopenia dengan melepaskan rangsangan katabolik interleukin-6 (IL-6) dan protein C-reaktif (CRP). Penelitian ini bertujuan untuk menentukan hubungan antara IL-6 dan kadar CRP terhadap parameter sarkopenia seperti massa otot, kekuatan pegangan, dan kecepatan berjalan.*

Metode: *Penelitian ini menggunakan desain cross-sectional analitik yang dilakukan di Desa Pedawa, Kabupaten Buleleng, Bali pada bulan Agustus 2016. Sekitar 79 responden berusia ≥ 60 tahun menggunakan teknik sampling acak stratifikasi. Variabel yang dinilai yaitu parameter sarkopenia (massa otot, kekuatan pegangan, dan kecepatan berjalan) termasuk IMT, serta IL-6 dan pemeriksaan tingkat CRP. Uji korelasi spearman dan parsial digunakan untuk menilai korelasi antara parameter IL-6, CRP, dan sarkopenia.*

Hasil: *Kadar IL-6 dan CRP tidak berkorelasi signifikan dengan tiga parameter sarkopenia. Kadar CRP berkorelasi dengan IL-6 (r = 0.37; p = 0.001) dan IMT (r = 0.29; p = 0.009). Pada kelompok pria, IL-6 hanya berkorelasi dengan CRP (r = 0.40; p = 0.011). Sedangkan pada kelompok wanita, IL-6 berkolerasi dengan CRP (r = 0.38; p = 0.017), kecepatan berjalan (r = 0.33; p = 0.037) serta CRP berkorelasi dengan IMT (r = 0.32; p = 0.049) dan massa otot total (r = -0.32; p = 0.043). Setelah penyesuaian untuk variabel IMT, IL-6 berkorelasi dengan CRP (r = 0.43; p = 0,001) dan massa otot total (r = -0.25; p = 0.026) serta secara signifikan berkorelasi pada kelompok kurus (IMT<18.5 kg/m^2) (r = -0.50; p = 0.026). CRP tidak berkorelasi secara signifikan dengan tiga parameter sarkopenia pada uji spearman, korelasi parsial, dan uji korelasi spesifik spearman berdasarkan pada kelompok IMT.*

Kesimpulan: *Kadar IL-6 berhubungan dengan penurunan massa otot total pada keseluruhan lansia desa Pedawa setelah penyesuaian variabel IMT.* ***(Health Science Journal of Indonesia 2018;9(1):37-44)***

Kata kunci: *IL-6, Protein C-Reaktif (CRP), Sarkopenia, Lanjut usia, Desa Pedawa.*

Abstract

Background: Sarcopenia is a syndrome characterized by decreased muscle mass with decreased muscle strength and or muscle function. Oxidative stress and inflammatory processes are known as triggering factors for sarcopenia by releasing catabolic stimuli of interleukin-6 (IL-6) and C-reactive protein (CRP).This study aims to determine the relationship between IL-6 and CRP levels to sarcopenia parameter such as muscle mass, grip strength, and walking speed.

Methods: This study was an analytic cross-sectional design conducted at Pedawa Village, Buleleng District, Bali in August 2016. About 79 respondents aged ≥ 60 years using stratified random sampling technique. The assessed variables were sarcopenia parameter (muscle mass, grip strength, and walking speed) including BMI, as well as IL-6 and CRP levels examination. Spearman and partial correlation test were used to assess the correlation among IL-6, CRP, and sarcopenia parameters.

Results: IL-6 levels and CRP were not significantly correlated with the three parameters of sarcopenia. CRP levels correlated with IL-6 (r = 0.37; p = 0.001) and BMI (r = 0.29; p = 0.009). In the male group, IL-6 was only correlated with CRP (r = 0.40; p = 0.011). While in the women group, IL-6 correlated with CRP (r = 0.38; p = 0.017), walking speed (r = 0.33; p = 0.037) and CRP correlated with BMI (r = 0.32; p = 0.049) and total muscle mass (r = -0.32; p = 0.043). After adjustment to BMI variable, IL-6 was correlated with CRP (r = 0,43; p = 0,001) and total muscle mass (r = -0.25; p = 0.026) and significantly correlated in underweight groups (BMI<18.5 kg/m^2) (r=-0.50; p=0.026). CRP was not significantly correlated with the three parameters of sarcopenia on Spearman, partial correlation, and Spearman's specific correlation test based on BMI group.

Conclusion: IL-6 levels were associated with total muscle mass loss after BMI adjustmentin Pedawa village's elderly as a whole. ***(Health Science Journal of Indonesia 2018;9(1):37-44)***

Keywords: IL-6, C-Reactive Protein (CRP), Sarcopenia, Elderly, Pedawa village.

In 2008 to 2040 there was an increase in the world population aged over 65 years by two-fold, from 7.8% to 14.7%.[1] According to the population census in 1990, the number of elderly individuals in Bali reached more than 230,000 people or 8.3 percent of the total Bali population. Then, in 2015 the number of population was expected to increase nearly twice compared to 1990 become more than 432,000 people.[2] In Bali, there are several places with indigenous peoples called the Bali Age Village located in Panglipuran Village (Bangli Regency), Trunyan Village (Karangasem Regency) and Pedewa Village (Buleleng Regency). One of them is Pedawa Village on the top of mountain in North of Bali. Pedawa Village is an isolated and inhabited village of Balinese indigenous people. This village has a specific population where genetic or host factors play an important role in the pathophysiology of a non-communicable disease. Previous research in Pedawa Village regarding non-communicable diseases related to the aging process obtained the prevalence of underweight by 18.6%, Diabetes Mellitus by 3.9%, systolic hypertension by 14.6% and diastolic hypertension by 12.2%.[3] high prevalence of underweight could be high prevalence of sarcopenia. In addition, there is a need for research on non-communicable diseases related to other aging processes, such as sarcopenia to get an overview of the specific elderly population.

The great change that occurs in old age is a progressive decline in skeletal muscle mass, which then leads to a decrease in muscle strength and functional ability. Loss of muscle mass and strength in aging (increasing age) is called sarcopenia. Sarcopenia is a syndrome characterized by a progressive and comprehensive loss of skeletal muscle mass and strength which poses a risk of physical disability, reduced quality of life, and death. There are several mechanisms involved in the onset and progression of sarcopenia.[4] The multifactorial processes that trigger sarcopenia include loss of alpha motor nerve inputs in the cytokines, physical activity, hormonal changes, energy, nutrition intake, oxidative stress, and inflammatory processes. There is evidence that such inflammatory mediators such as tumor necrosis factor alpha (TNF-α), interleukin (IL-6) and C-reactive proteins interact with the hormonal changes inherent to aging, thus causing a decline in physical activity and fat replacement of muscles, which simultaneously lead to volumetric muscle loss.[5,6] Subclinical inflammation and oxidative stress in the sarcopenia mechanism trigger the release of catabolic stimuli such as interleukin-6 (IL-6), ciliary neurotropic factor (CNTF) and tumor necrosis factor (TNF). Cellular IL-6 is a significant predictor of sarcopenia.[7] IL-6 might trigger muscle atrophy characterized by loss of myofibrillar protein.[6] The results of studies in elderly women showed elevated levels of IL-6 due to sarcopenia.[8] In addition, there is a significant relationship between high CRP levels and sarcopenia.[9] Increased levels of IL-6 and CRP may increase the risk of losing muscle strength.[10]

Based on the information above, this study aims to know the relationship between IL-6 and CRP levels with the three parameters of sarcopenia such as muscle mass, grip strength, and walking speed in specific population, indigenous and isolated place. This study is still rarely performed or published in Indonesia. The results of this study are expected to be a reference for preventive and curative interventions of sarcopenia in the future.

METHODS

Study design and samples

This cross-sectional analytic study was conducted in Pedawa Village, Buleleng District, Bali in August 2016 using stratified random sampling of 600 elderly population spread over 6 hamlets. The respondents were people with greater age or equal 60 years of cooperative attitudes without any comorbidities enrolled in the study (n = 79). The exclusion criteria include subjects with malignancy; suffering from acute infection; heart failure; chronic liver disease; kidney failure stage 4 and 5; taking corticosteroids; aspirin or NSAIDs for at least two weeks; immobility or Barthel Activity Daily life scores less than 9; suffering from sequelae; severe cognitive damage; and experience an inability to be interviewed due to socio-linguistic problems and / or aphasia. Other comorbidities were controlled by analysis.The elderly individuals were explained the purpose of the study and had obtained informed consent.

Data collection

Data were collected through interview method, anthropometric and Bioelectrical Impedance Analysis (BIA) measurement, grip strength, walking speed, examination of IL-6 and CRP serum levels at one time.

Anthropometry and body fat percentage

The anthropometric examination was performed by body weight (BW) and height (H) measurement based on knee height. Body height measurement (cm) in the elderly using knee height was carried out by knee height gauge, then converted through calculation of Chumlea knee height formula.[11] The waist and hip circumference were measured using a cloth tape measure in centimeters (cm). BMI was calculated using the Omron BIA then categorized based on WHO criteria with some modifications into three groups namely underweight (BMI < 18.5 kg/m2), normal (18.5 < BMI < 24.9 kg/m2), as well as overweight and obese (BMI > 25 kg/m2).[12] The body fat percentage was obtained through BIA measurement.

Sarcopenia parameter

Based on the Asian Working Group for Sarcopenia (AWGS) recommendation, sarcopenia parameters measured in this study were muscle mass, grip strength, and walking speed.[11] The muscle mass measurements using BIA tools obtained total skeletal muscle mass (upper limb muscle mass, lower limbs, and trunk) in percent (%). The grip strength (muscle power) examination was performed with the aid of a handheld dynamometer, expressed in kilograms (kg). Walking speed (m / s) was calculated with a run test as far as 4.57 meters.

IL-6 and CRP levels

The levels of IL-6 and CRP were derived and examined from blood serum. Approximately 5 mL of venous blood subject taken by researchers assistant (phlebotomist). The procedure was performed by a qualified professional in the morning (between 8:00 and 10:00) to avoid the influence of circadian cycle changes. The blood in the serum centrifuge is kept below 0°C by dry ice and taken to the laboratory. IL-6 and CRP concentrations were analyzed using the Quantikine HS Human IL-6 Immunoassay reagent (HS Catalog of HS600B) and Quantikine Human CRP Immonoassay (Catalog of DCRP00) Examination of IL-6 and CRP using Quantikine HS Human IL-6 Immunoassay (HS600B Catalog Listing) and Quantikine Human CRP Immonoassay (DCRP00 Catalog Number) were measured by Enzyme-linked immunosorbent assay (ELISA) method with pg / mL unit. This measurement is done one time without repetition.

Statistical analysis

The descriptive statistical analysis was performed using measures of central tendency (mean and median) and variability (range and standard deviation). The data distribution wasn't normal so that Spearman correlation test was used to measure the correlation between numerical variables. A partial correlation test was applied to determine the correlation between IL-6 and CRP to the sarcopenia parameters by adjusting the BMI variable, considering a significance level (α) of 0.05. Statistical analyses were carried out using the Statistical Package for Social Sciences. (SPSS; version 16.0, Windows environment).

Ethical clearance

Ethical clearance has been obtained from the Ethics Committee of Research and Development Unit, Faculty of Medicine Udayana University / Sanglah Hospital with letter number: 1814/UN.14.2/ Litbang/2016

RESULTS

A total of 79 elderly participants participated in this study which included 40 males (50.6%) and 39 females (49.4%). Based on BMI, 20 subjects (25.3%) were classified as underweight, 41 subjects (51.9%) normal, and 18 subjects (22.8%) as overweight and obese. According to the sarcopenia parameters, (Table 1).

Table 1. Sample Characteristics of Study

Variables	Values
Age (years)	69.52 ± 8.71
Body Mass Index (kg/m^2)[1]	19.54 ± 4.659
Body height based on knee height (cm)	161.83 ± 6.3
Body weight (kg)	52.64 ± 12.31
Waist circumference (cm)	77.47 ± 13.66
Hip circumference (cm)	86.94 ± 1.38
Body fat (%)[2]	28.68 ± 7.82
Visceral fat (%)[2]	7.90 ± 6.25
Total skeletal muscle mass (%)[2]	89.03 ± 1.46
Upper Limb (%)[2]	30.40 ± 5.96
Lower Limb (%)[2]	39.33 ± 6.14
Truncal (%)[2]	19.30 ± 3.85
Grip strength (kg)	19.86 ± 7.13
Walking speed (m/s)	1.98 ± 0.60
IL-6[3]	1.42
CRP[3]	0.76

[1] Mean ± SD.

[2]Assessed with BIA.

[3] Median. IL-6 and CRP data were not normally distributed

The correlation between IL-6 and CRP with component and related sarcopenia parameters

The study found no significant correlation between IL-6 and CRP with sarcopenia parameters (muscle mass, grip strength, and walking speed) in Spearman correlation test, but obtained a significant correlation between IL-6 with CRP (r = 0.37, p = 0.001) and CRP with BMI (r = 0.29, p = 0.009). (Table 2 and 3)

Table 2. Correlation between IL-6 levels with component and related sarcopenia parameters.

Variables	IL-6		
	r	P	95% CI
Age	0.08	0.476	-0.143 – 0.295
Sex	0.10	0.365	-0.123 – 0.314
BMI	0.12	0.301	-0.103 – 0.332
CRP	0.37	0.001*	0.163 – 0.546
Total skeletal muscle mass (%)	-0.17	0.126	-0.375 – 0.053
Grip strength (kg)	-0.08	0.550	-0.295 – 0.143
Walking speed (m/s)	0.07	0.545	-0.153 – 0.286

*significant, p-value < 0.05

In each sex group, a correlation analysis of the sarcopenia parameter was performed. In the male sex group, there was a significant correlation between IL-6 level and CRP (r = 0.40, p = 0.011). whereas in the female sex group there was a significant correlation between IL-6 and CRP levels (r = 0.38, p = 0.017), IL-6 with walking speed (r = 0.33, p = 0.037), CRP with BMI (r = 0.32, p = 0.049), and CRP with total skeletal muscle mass (r = -0.32, p = 0.043). (Tables 4 and 5)

Table 3. Correlation between CRP levels with component and related sarcopenia parameters.

Variables	CRP		
	r	p	95% CI
Age	-0.06	0.586	-0.277 – 0.163
Sex	-0.08	0.499	-0.295 – 0.143
BMI	0.29	0.009*	0.074 – 0.480
IL-6	0.37	0.001*	0.163 – 0.546
Total skeletal muscle mass (%)	-0.10	0.388	-0.314 – 0.123
Grip strength (kg)	0.07	0.550	-0.153 – 0.286
Walking speed (m/s)	0.07	0.336	-0.153 – 0.286

*significant, p-value < 0.05

Table 4. Correlations between IL-6 levels and CRP with sarcopenia parameters in elderly men

Variables	IL-6			CRP		
	r	p	95% CI	r	p	95% CI
Age	-0.63	0.697	-0.787 - (-0.397)	-0.18	0.270	-0.465 – 0.139
BMI	0.31	0.053	-0.001 – 0.566	0.29	0.074	-0.023 – 0.551
IL-6	-	-	-	0.40	0.011*	0.102 – 0.632
CRP	0.40	0.011*	0.102 – 0.632	-	-	-
Total skeletal muscle mass (%)	-0.20	0.204	-0.481 – 0.118	-0.12	0.472	-0.415 – 0.198
Grip strength (kg)	0.05	0.747	-0.265 – 0.355	0.12	0.473	-0.198 – 0.415
Walking speed (m/s)	-0.20	0.213	-0.481 – 0.118	-0.30	0.059	-0.559 – 0.012

*significant, p-value < 0.05

Table 5. Correlation between IL-6 levels and CRP with sarcopenia parameters in elderly women

Variables	IL-6			CRP		
	r	p	95% CI	r	p	95% CI
Age	0.25	0.120	-0.071 – 0.524	0.01	0.973	-0.306 – 0.324
BMI	-0.02	0.880	-0.333 – 0.297	0.32	0.049*	0.005 – 0.577
IL-6	-	-	-	0.38	0.017*	0.074 – 0.621
CRP	0.38	0.017*	0.074 – 0.621	-	-	-
Total skeletal muscle mass (%)	-0.22	0.178	-0.500 – 0.102	-0.32	0.043*	-0.577 – (-0.005)
Grip strength (kg)	-0.10	0.528	-0.402 – 0.222	-0.79	0.638	-0.884 – (-0.633)
Walking speed (m/s)	0.33	0.037*	0.017 – 0.584	0.08	0.624	-0.241 – 0.385

*significant, p-value < 0.05

The scatter plot diagram aims to determine the relationship pattern between BMI and IL-6 as well as to predict whether a non-significant relationship between IL-6 and the three sarcopenia parameters are due to the presence of the BMI variable. The diagram showed that high distribution of IL-6 appears trend at low and high BMI values (Figure 1).

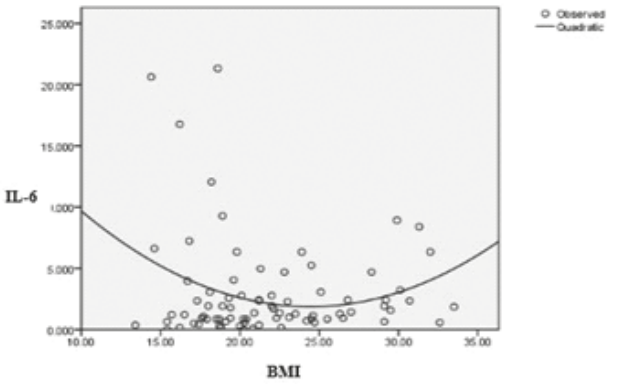

Figure 1. Scatter plot diagram of BMI dan IL-6 variables

Correlation between IL-6 and CRP on specific sarcopenia parameters based on BMI group

Based on the assumption that BMI variable influences a significant correlation between IL-6 and CRP with sarcopenia parameter, partial correlation test was performed between IL-6 and CRP with related sarcopenia parameter by adjusting BMI variable. Partial correlation test by adjusting BMI suggest that IL-6 variable still showed significant correlation with CRP ($r = 0.43$, $p < 0.001$) (Table 6).

Table 6. Partial correlation between IL-6 with sarcopenia parameter (adjusted for BMI variable).

Controlled Variable	Variables	IL-6		
		r	p	95% CI
BMI	CRP	0.43	0.001*	0.163 – 0.546
	Total skeletal muscle mass (%)	-0.25	0.026*	-0.446 – (-0.031)
	Grip strength (kg)	-0.14	0.211	-0.350 – 0.083
	Walking speed (m/s)	0.14	0.226	-0.083 – 0.350

*significant, p-value < 0.05

The result of partial correlation test between IL-6 and related sarcopenia parameter after adjusting for BMI variable showed significant correlation to total skeletal muscle mass. but CRP is not significantly associated with sarcopenia parameters. Then, we performed a separate Spearman correlation test based on BMI group (underweight, normal, and overweight-obese) (Table 7). In all three BMI groups, there is a significant negative correlation between IL-6 and total skeletal muscle mass in the underweight group ($P < 0.05$).

DISCUSSION

Sarcopenia associated with aging is a slow, progressive, and seemingly inevitable process. This directly affects the functional capacity of elderly individuals and leads to a decline in health. This condition will directly affect the functional capacity of elderly individuals and lead to a decrease in health.[13]

Table 7. Correlation between IL-6 and CRP with specific sarcopenia parameters in BMI group

BMI Group	IL-6			CRP		
	r	p	95% CI	r	p	95% CI
Underweight Group						
Total Skeletal Muscle Mass (%)[2]	-0.50	0.026*	-0.771 – (-0.074)	-0.15	0.539	-0.555 – 0.313
Grip strength (kg)	-0.33	0.162	-0.674 – 0.131	-0.05	0.818	-0.481 – 0.401
Walking speed(m/s)	0.37	0.108	-0.086 – 0.698	0.11	0.652	-0.349 – 0.526
Normal Group						
Total Skeletal Muscle Mass (%)[2]	0.04	0.981	-0.27 – 0.343	-0.06	0.711	-0.360 – 0.252
Grip strength (kg)	-0.11	0.478	-0.403 – 0.204	-0.05	0.770	-0.352 – 0.261
Walking speed(m/s)	0.02	0.897	-0.289 – 0.325	-0.07	0.660	-0.369 – 0.242
Overweight and Obesity Group						
Total Skeletal Muscla Mass (%)[2]	-0.09	0.726	-0.534 – 0.393	0.12	0.627	-0.367 – 0.555
Grip strength (kg)	0.16	0.512	-0.331 – 0.583	0.06	0.798	-0.418 – 0.512
Walking speed(m/s)	0.03	0.888	-0.443 - 0.490	-0.20	0.408	-0.609 – 0.431

*significant, p-value < 0.05

This study aims to determine the relationship between IL-6 and CRP with sarcopenia parameters. Prior to statistical adjustment for BMI variables, we found no significant correlation between IL-6 and CRP with three sarcopenia parameters. To see more detailed results we do analysis by sex. In the male sex group, there was a significant coefficient on IL-6 with CRP. In the female sex group, there was a positive correlation between IL-6 with CRP, walking speed and CRP with BMI and negative correlation with CRP with skeletal muscle mass. A study conducted on 130 elderly women found a significant correlation between IL-6 levels with functional muscle.[14] In the study by Choi et al (2013), it was found out that BMI was associated with CRP levels and the relationship was greater in women than in adult males.[15] The negative association between CRP levels and skeletal muscle mass was found in a study of 118 elderly women and was found to be significantly higher in CRP in older people with lower muscle mass than those with normal muscle mass.[16] CRP affects muscle cell size through the MPS pathway mechanism. [16]

After adjusting the BMI variable, partial correlation test was obtained a significantcorrelation between IL-6 and muscle mass (weak negative correlation). These results are consistent with research conducted by Haren et al (2010) who found that an increase in IL 6 leads to a loss of muscle mass.[17] However, the study also showed that elevated levels of IL-6 will lead to decreased muscle function, while our study found no association between IL-6 and muscle function (walking speed).[17]

One of the underlying mechanisms of mass muscle reduction in high-IL-6 levels is muscle atrophy induced by elevated levels of IL-6.[18] Besides the effect of muscular atrophy, another theory that allegedly underlies decrease of mass muscle decline is a catabolic state induced by IL-6 in muscle. However, this catabolic state is often found only in sophisticated systemic conditions such as sepsis or cachexia.[18,19]

In our specific analysis based on BMI groups, a significant relationship between IL-6 and muscle mass was consistently found in the BMI underweight group (moderately negative correlation). Non-significant relationships were found in normal BMI and overweight-obesity groups. The high IL-6 distribution in subjects with low BMI scores was depicted in the scatter plot chart. This is an important note to us that keeping the elderly from underweight conditions will allow them to avoid the muscle mass loss due to IL-6, so as to prevent the onset of sarcopenia. These data can be a reference for clinicians to consider the BMI modification in elderly individuals.

IL-6 was significantly associated with CRP (positive correlation) in partial correlation test by adjusting BMI and Spearman correlation test without adjusting for BMI variables. This result is similar to a study performed by Il'Yasova, et al. (2008), which suggests a positive correlation between IL-6 and CRP levels.[20] IL-6 is responsible for triggering the synthesis of acute phase proteins such as CRP theoretically.[21] However, the correlation between IL-6 and CRP did not become significant when a specific analysis was performed based on the BMI group in our study.

Although there is a correlation between IL-6 with a reduction in CRP, our study did not find any correlation between CRP and the sarcopenia parameters, particularly in muscle mass and grip strength. This indicates that CRP does not mediate the role of IL-6 in the mass muscle decline. The results of our study differed from a prior study conducted by Atkins et al. (2014),who reported that CRP levels were positively related to low muscle mass, regardless of the effect of age, lifestyle, and body composition.[22] In addition, it is also demonstrated that there was a pivotal role of increased CRP level in the muscle strength reduction.[9]

The conflicting results observed in studies are probably due to the differences in sample characteristics, such as comorbidities, socioeconomic status, education level, and physical activity level. In this study, the sample size is relatively small (n = 79) that a specific correlation test based on BMI group could not be carried out optimally in each group of BMI. This can be seen from the inconsistent relationship between IL-6 and CRP in which the correlation between the two variables becomes insignificant when a specific correlation test was performed for each BMI group. Therefore, similar studies in the future are expected to use larger samples. Another our study limitation is the exclusion of several variables suspected to be associated with sarcopenia parameters into data analyzes such as nutritional intake (protein, fat, carbohydrates) and the amount of energy/calorie use. In this context, we did not explicitly perform a linear regression to determine the relationship between nutritional intake, energy use, IL-6, and CRP with

sarcopenia parameters. Besides, the cross-sectional design does not allow causal inferences about the relationships between the studied variables.

In conclusion, in the elderly men group IL-6 correlated with CRP, whereas in the elderly women group IL-6 had a positive correlation with CRP, BMI and walking speed and CRP negatively correlated with total muscle mass. IL-6 levels were correlated with the decrease in total muscle mass of Pedawa village elders as a whole after adjustment of BMI variables.

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REFERENCES

1. Schoeni RF, Ofstedal MB. Key themes in research on the demography of aging. Demography [Serial online]. 2010 [cited 2017 December 28];47(S):S5–15. Available from: http://link.springer.com/10.1353/dem.2010.0001
2. Rimbawan ND. Profil lansia di Bali kaitannya dengan pembangunan. Piramida [Serial online]. 2007 [cited 2017 December 28];1–11. Available from: https://ojs.unud.ac.id/index.php/piramida/article/view/2980
3. Budhiart A, Aryana IS. Hubungan Obesitas dengan Diabetes Melitus dan Hipertensi pada penduduk Baliage di desa Pedawa, Buleleng, Bali. Medicina (B Aires) [Serial online]. 2012 [cited 2017 December 28];38:2540–8321. Available from: https://ojs.unud.ac.id/index.php/medicina/article/view/3278
4. Jentoft AJC, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia : European consensus on definition and diagnosis. Age Ageing. 2010;39(4):412–23.
5. Jensen GL. Inflammation: roles in aging and Sarcopenia. JPEN J Parenter Enter Nutr. 2008;32:656–9.
6. Pal M, Febbraio MA, Whitham M. From cytokine to myokine : the emerging role of interleukin-6 in metabolic regulation. Immunol Cell Biol [Serial online]. 2014 [cited 2017 Dec 28];92(4):331–9. Available from: http://dx.doi.org/10.1038/icb.2014.16
7. Morley JE. Sarcopenia in the elderly. Fam Pract. 2012;29:i44–8.
8. Pereira LSM, Narciso FMS, Oliveira DMG, Coelho FM, Souza D da G de, Dias RC. Correlation between manual muscle strength and interleukin-6 (IL-6) plasma levels in elderly community-dwelling women. Arch Gerontol Geriatr. 2009;48(3):313–6.
9. Bano G, Trevisan C, Carraro S, Solmi M, Luchini C, Stubbs B, et al. Inflammation and sarcopenia: a systematic review and meta-analysis. Maturitas. 2017;96:10–5.
10. Stenholm S, Harris T, Rantenen T, Visser M, Kritchevsky SB, Ferrucci L. Sarcopenic obesity-definition,etiology and consequences. Curr Opin Clin Nutr Metab Care. 2008;11(6):693–700.
11. EA M, N P, Yudomurti. Tinggi badan yang diukur dan berdasarkan tinggi lutut menggunakan rumus chumlea pada lansia. Med Indones. 2012;49:1–6.
12. Fujikawa H, Araki T, Okita Y, Kondo S, Kawamura M, Hiro J, et al. Impact of Sarcopenia on surgical site infection after restorative proctocolectomy for ulcerative colitis. Surg Today. 2017;47(1):92–8.
13. Brotto M. Aging, sarcopenia and store-operated calcium entry. A common link? Cell Cycle. 2011;10(24):4201–2.
14. Pereira DS, Cipriano VF, Amorim JSC, Queiroz BZ, Felício DC, Pereira LSM. Handgrip strength, functionality and plasma levels of {IL}-6 in elderly women. Fisioter em Mov [Serial online]. 2015 [cited 2018 March 1];28(3):477–83. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0103-51502015000300477&lang=pt
15. Choi J, Joseph L, Pilote L. Obesity and C-reactive protein in various populations: a systematic review and meta-analysis. Vol. 14, Obesity Reviews. 2013. p. 232–44.
16. Wåhlin-Larsson B, Wilkinson DJ, Strandberg E, Hosford-Donovan A, Atherton PJ, Kadi F. Mechanistic links underlying the impact of C-reactive protein on muscle mass in elderly. Cell Physiol Biochem. 2017;44(1):267–78.
17. Haren MT, Malmstrom TK, Miller DK, Patrick P, Perry HM, Herning MM, et al. Higher C-reactive protein and soluble tumor necrosis factor receptor levels are associated with poor physical function and disability: a cross-sectional analysis of a cohort of late middle-aged african Americans. Journals Gerontol - Ser A Biol Sci Med Sci. 2010;65 A(3):274–81.
18. Carson J, Baltgalvis K. Interleukin-6 as a key regulator of muscle mass during cachexia. Exerc Sport Sci Rev [Serial online]. 2010 [cited 2018 March 1];38(4):168–76. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065300/
19. Chen LK, Liu LK, Woo J, Assantachai P, Auyeung TW, Bahyah KS, et al. Sarcopenia in Asia: consensus report of the Asian working group for Sarcopenia. J Am Med Dir Assoc [serial online]. 2014 [cited 2018 March 1];15(2):95–101. Available from: http://dx.doi.org/10.1016/j.jamda.2013.11.025
20. Il'yasova D, Ivanova A, Morrow JD, Cesari M, Pahor M. Correlation between two markers of inflammation, serum C-reactive protein and interleukin 6, and indices of oxidative stress in patients with high risk of cardiovascular disease. Biomarkers [serial online]. 2008 [cited 2018 March 1];13(1):41–51.

Available from: http://informahealthcare.com/doi/pdfplus/10.1080/13547500701617708

21. Tanaka T, Narazaki M, Kishimoto T. Il-6 in inflammation, immunity, and disease. Cold Spring Harb Perspect Biol. 2014;6(10).
22. Atkins JL, Whincup PH, Morris RW, Wannamethee SG. Low muscle mass in older men: The role of lifestyle, diet and cardiovascular risk factors. J Nutr Heal Aging. 2014;18(1):26–33.