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ORIGINAL ARTICLE

Low subcutaneous fat as a risk factor for sarcopenia among elderly women in Bali, Indonesia

a community-based age-matched case-control study

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Background

This study aimed to examine risk factors of sarcopenia among elderly females in Bali after matching for each age group.

Methods

A Balinese community age-matched case-control study was conducted by randomly selecting 39 elderly women with sarcopenia using The European Working Group in Older People 2 (EWGSOP 2) 2018 criteria and 39 participants without sarcopenia.

Results

The present study has found that body mass index (underweight), whole-body subcutaneous fat, the percentage of body fat, whole-body skeletal muscle have effects on sarcopenia. The multivariate conditional logistic regression analysis showed a significant increase in the risk of sarcopenia for participants with a lower percentage of whole-body subcutaneous tissue (odds ratio:20.00, 95% confidence interval: 2.68-149.02). Redistribution of lipid from subcutaneous adipose tissue (SAT) to visceral adipose tissue in menopausal women has caused the aging-related programmed loss of brown adipocytes in the SAT, caused an increase in pro-inflammatory adipokines and a decrease in anti-inflammatory mediators, and contributed to sarcopenia through various mechanisms, such as insulin resistance, the disruption protein synthesis, and the inhibition of myoblast differentiation. Myokines produced by skeletal muscle, such as Irisin can facilitate the browning of white adipose tissue (WAT) and promote the increase of subcutaneous fat.

Conclusion

Our study found that the low percentage of whole-body subcutaneous fat is a potent risk factor for sarcopenia.

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Sarcopenia is a progressive age-related disease characterized by the presence of low muscle strength and low quality or quantity of muscle.[1] This disease has devastating impacts on health and finance. In terms of health, sarcopenia causes an increased risk of falls and fractures, disruption to daily activities, an increase in the occurrence of heart disease, respiration disease, cognitive impairment, and mobility disorders.[1,2] Besides, health costs due to sarcopenia were estimated at approximately US$ 860 for each male case and US$ 933 for each female case in the United States in 2000.[3]

The prevalence of sarcopenia in the elderly community was quite varied, ranging from 1-29% in males and up to 30% in females.[4] As age increases, the prevalence also increases from 5-13% in those aged 60-70 years old to 11-50% in those aged more than 80 years old.[5,6] In terms of gender, sarcopenia was more commonly found in females for those aged less than 75 years old and in males for those aged more than 75 years old.[7]

Over the last decades, the proportion of elderly in Indonesia has grown significantly from 4% in 1917 to 8.97% in 2017.[8] In terms of gender, female elders have a larger proportion compared to the male ones (9.47% to 8.48%).[8] Compared to the 70-79 years old group and the 80+ years old group, the elderly aged 60-69 years old had the highest percentage (5.65% of all population) of elderly in Indonesia in 2017.[8] Bali has one of the highest proportions of elderly in Indonesia (10.79% of all population).[8] Since majority elderly population in Bali lived in urban, the prevalence of sarcopenia was higher for those lived in urban area compared to those in rural area in Bali (48.2% vs 27.1%). Since sex hormone has a potential role in pathophysiology of sarcopenia, we aimed to examine the prevalence of and risk factors of sarcopenia among elderly females in Bali after matching for each age group.

METHODS

This study was conducted in Bali province, Indonesia. Our study used stratified sampling in determining study locations. Therefore, four villages in four districts in Bali were being chosen as study locations.

Study Population

All female elders, who were aged 60 years and older, resided in four villages in four districts in Bali province, Indonesia during the period between August 1, 2016, and September 30, 2018, were included in this present study. In addition, the participants should able to mobilize and have no active infections within the previous month or malignancies. After explaining the detail of the study, they need to have adequate cognitive function to be able to complete a written consent form indicating their agreement to participate in the study. Exclusion criteria for this study are the inability to fullfill the inclusion criteria or unable to complete the written consent form due to serious cognitive impairment and inability to have muscle mass and grip strength being measured. 245 participants met the inclusion and exclusion criteria, and 237 (96.7%) consented to enrolment.

Case Selection

Sarcopenia is a progressive disease that is characterized with generalized loss of skeletal muscle mass and strength, and accompanied with impaired physical performance.[9] The European Working Group in Older People 2 (EWGSOP 2) in 2018 was adapted as diagnostic criteria in which requires the presence of both low muscle strength and low muscle quality or quantity (muscle mass).[1]

Muscle Strength Assessment

In this research, handgrip strength was being assessed by using a hand-held dynamometer, (expressed in kilogram) to measure muscle strength. The strength was measured using the patients' dominant hand three times and the highest value was used to measure the patient's muscle strength. The use of handgrip strength was also recommended by The Sarcopenia Definition and Outcome Consortium.[10] Having hand grip strength less than 18 kg was classified as having low muscle strength in this study.[11]

Muscle Mass Assessment

In this study, muscle mass was being measured using bioelectrical impedance analysis (BIA) (ohms, W). During BIA measurement, participants stood in a supine position. Then, muscle mass was estimated using the BIA equation of Janssen, Shepard.[3]

Skeletal Muscle Mass Index =
(skeletal muscle mass / weight) x100

In the present study, the low muscle mass was defined as having a skeletal muscle mass index of less than 6.42 kg/m2.[11]

Control Selection

A control was defined as a participant without sarcopenia. Controls were individually matched with each case for the age group (60-70, 70-80, more than

80 years old). Then, matched controls were being randomly chosen to meet the ratio 1:1 with the case for each age group.

Data Collection

The data of basic characteristics, such as hypertension status, body weight, and height, were collected from both case and control participants. Those who have blood pressure equal to or more than 140 / 90 mmHg or taking antihypertensive agents, were defined as having hypertensive disease.[12]

Anthropometric Measurement

Bodyweight (to the nearest 0.1 kg) was measured in kilograms while height (to the nearest 0.1 cm) was measured in centimeters. During weight and height measurement, participants used light clothing and without shoes. Body Mass Index (BMI, in kg/m2) was calculated accordingly. After that, underweight and obesity status were defined using WHO criteria (Underweight: BMI < 18.5 kg/m2; Obesity: BMI >30).[13]

Body Composition Measurement

Bioelectrical impedance analysis (BIA) was being used to measure body composition, which is being measured as body fat and skeletal muscle mass. The percentage of body fat was derived from resistance values through equations from Chumlea, Guo [14] and the estimation using an equation from Janssen, Baumgartner [15] was used to measure skeletal muscle mass. Percentage of Subcutaneous fat is being considered normal if it was within 20-35%.

Statistical Analysis

The algorithm developed by the European Working Group in Older People 2 (EWGSOP 2) in 2018 was used to identify participants with sarcopenia.[1] We adjusted the data according to age to control age as a potential confounder in our study design. Data were analyzed to obtain descriptive statistics. Continuous variables were being presented as mean if the data were in normal distribution and being presented as median if the data were not normally distributed. Initially each potential risk factor was being analysed using univariate analysis. Those with with P<0.05 in the univariate analysis were then included in the models in the multivariate analysis using the backward regression models. A P value less than 0.05 was considered statistically significant. All p values were two-tailed. All analyses were performed using the SPSS 16.0 package (SPSS Inc., Chicago, IL).

Ethical Consideration

Ethical approval was obtained from the Udayana University Faculty of Medicine. After by being explained the detail of the study and reading the information sheet, informed consent (verbal and written) was voluntary collected from each participant. Non-identifiable identification codes were assigned to all participants for data entry and data analysis. None of the participants can be identified in the report writing or publication.

RESULTS

In this matched case-control study, 245 participants were invited to participate and 237 participants consented to enrolment. Cases were participants with sarcopenia who have met the diagnostic criteria from the European Working Group in Older People 2 (EWGSOP 2) in 2018 and control were participants who have not met the criteria. In the present study, we found a total of 39 participants with sarcopenia. The prevalence of sarcopenia was 16.46% among elders. The prevalence was 14.1% among elders aged 60-70 and increased to 18.9% among those aged 70-80, and 22.2% among those aged 80 and over. Then, every 39 cases and 39 controls, individually matched with cases (1:1) on age for each age group (60-70, 70-80, and more than 80 years old). The mean (SD) age (years) was 70.64 (9.56) and 69.82 (8.25) for cases and control respectively. The distribution of demographic characteristics, such as hypertension status, body mass index, the district of living, and relative distribution of potential risk factors in cases and controls are shown in Table 1 and Table 2. The present study has found that body mass index (being underweight), low level of whole-body subcutaneous fat, the percentage of body fat, whole-body skeletal muscle have effects on sarcopenia. The odd of the underweight status of participants was 2.99 higher among cases with sarcopenia compared to controls who did not have the disease (95% Confidence Interval [95% CI]: 1.10 to 8.16) (Table 1).

In the univariate analysis, we found that being underweight, the percentage of body fat, the percentage of subcutaneous fat in the whole body, and the lower percentage of subcutaneous fat in the whole body have significant effects on sarcopenia (Table 2). Therefore, we included them in our multivariate analysis. In the multivariate analysis, we found that only the lower percentage of subcutaneous fat in the whole body is significantly associated with sarcopenia (Table 2).

Table 1 *Characteristic of Respondents*

Characteristic	Sarcopenia	Not sarcopenia	Total
Gender (female)	39	39	78
Age group			
60-70 years old	18	18	36
70-80 years old	15	15	30
More than 80 years old	6	6	12
Hypertension status			
Hypertension	20	17	37
Not hypertension	19	22	41
Body mass index			
Underweight	17	8	25
Normal	14	22	36
Overweight and obesity	8	9	17
Skeletal muscle	mean	mean	difference
Arm	27.87%	25.18%	2.69%
Leg	34.54%	34.52%	0.02%
Trunk	17.57%	16.12%	1.46%
Whole body (%)	20.12%	27.25%	-7.14%
District of living			
Buleleng	19	19	38
Denpasar	2	11	13
Klungkung	7	4	11
Tabanan	11	5	16

Table 2 *Conditional logistic regression analysis to estimate the odds of sarcopenia in elderly women*

Variable	Univariate odd ratio (95% CI)	P	Multivariate odd ratio (95% CI)	P
Underweight				
Being underweight	3.25 (1.06-9.97)	***0.04***	1.86 (0.35-9.87)	0.46
Not being underweight	1.0 (reference)		1.0 (reference)	
Obesity				
Obese	1.00 (0.06-15.99)	1.00		
Not obese	1.0 (reference)			
Visceral fat (%)	0.95 (0.88-1.02)	0.14		
Subcutaneous fat in the whole body (%)				
Normal percentage	1.0 (reference)	***<0.01***	1.0 (reference)	***<0.01***
Lower percentage	20 (2.68-149.02)		20 (2.68-149.02)	
Ratio visceral fat per subcutaneous fat	0.45 (0.06-3.28)	0.43		
Percentage of body fat	0.89 (0.82-0.98)	***0.01***	1.13 (0.85-1.49)	0.40
Resting metabolism	1.00 (0.99-1.00)	***0.01***		

DISCUSSION

In the present study, we estimated the prevalence of sarcopenia and its association with body composition measurement in female elderly communities in Bali Province. Our study has found that the prevalence of sarcopenia found in Bali Province was 16.46% and the prevalence increases with increasing age from 14.06% in those aged 60-70 years old to 22.22% in those aged more than 80 years old. Our study result on the prevalence of sarcopenia was in line with other previous studies in the elderly community that increasing age is a risk factor of developing sarcopenia.[4-6,16] Therefore, we matched each participant with sarcopenia with their respective controls according to the age group to control the effect of the age group by design.

Our univariate analysis found that being underweight, the percentage of fat, subcutaneous fat in the arm and whole body, and the low percentage of whole-body subcutaneous fat have significant effects on sarcopenia (Table 2). Surprisingly, the low whole body subcutaneous fat was the only risk factor found that is associated with an increased risk of sarcopenia in elderly women.

Even though various studies, such as Lau, Lynn[17], Sazlina, Lee[18], has shown that underweight status is a potent risk factor for sarcopenia, our study found the opposite result (Table 2). One of the possible reasons is that our study adjusted the underweight status according to age and gender. It seems that age-matching for each case and control group can show that underweight status may not a significant risk factor for sarcopenia among elderly women.

Although the percentage of fat and subcutaneous fat in the arm and whole body have significant effects on sarcopenia in our univariate analysis (Table 2), the current study found that only the low percentage of whole-body subcutaneous fat is significantly associated with sarcopenia (Table 2). Possible mechanism of how low subcutaneous fat in the older person influence sarcopenia and the possible intervention that can be done to alleviate the effect of sarcopenia.

The next paragraphs will discuss the possible mechanism of how low subcutaneous fat in the aged person influence sarcopenia and the possible interventions that be done to alleviate the effect of sarcopenia.

The ageing process in menopausal women has caused the redistribution of lipid from subcutaneous adipose tissue (SAT) to visceral adipose tissue (VAT). This distribution has been known to be closely associated with the development of sarcopenia, metabolic syndrome, and insulin resistance.[19] One of the reasons is that the ageing-related programmed loss of brown adipocytes in the SAT.[20] Brown adipocytes, known as energy-consuming adipocytes, can produce signals (adipokines) to different organs and tissue. Therefore, the redistribution of lipid has caused an increase in pro-inflammatory adipokines, such as Leptin, IL-6, and TNF-α, and a decrease in anti-inflammatory mediators, such as Adiponectin and Vaspin (Visceral adipose tissue-derived serine protease inhibitor) [21] (Figure 1).

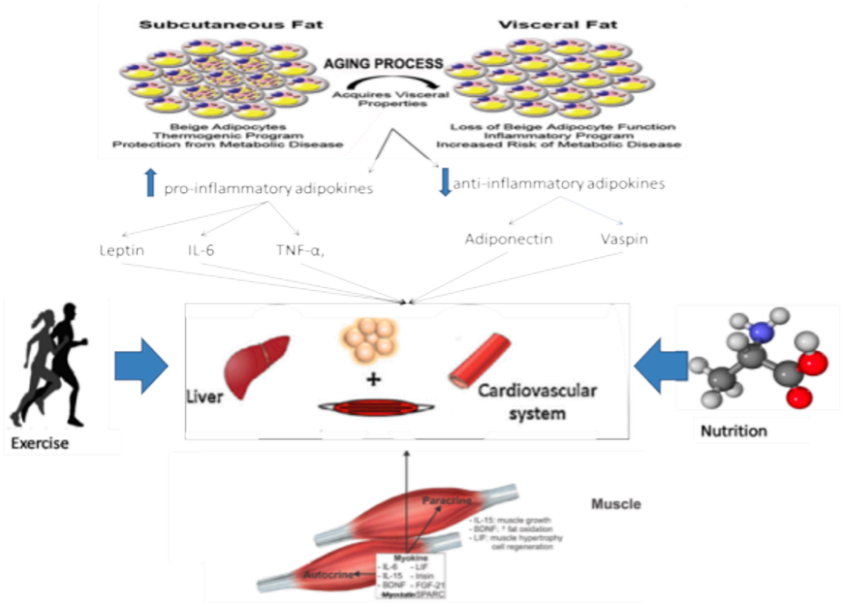

Figure 1 *Muscle-Adipose Axis: The ageing process in menopausal women has caused the redistribution of lipid from subcutaneous adipose tissue (SAT) to visceral adipose tissue (VAT). This redistribution has increased pro inflammatory adipokines and decreased anti-inflammatory adipokines, which then can contribute to sarcopenia through various myokines, adipokines, and cytokines in liver, adipose tissue, muscle tissue, and cardiovascular tissue. Exercise and nutrition can alleviate sarcopenia through various mechanisms.*

The increase of pro-inflammatory adipokines contributes to sarcopenia through various mechanisms. Skeletal muscle can be regulated by leptin through the process of AMPK modulation. The increase in leptin was associated with muscle atrophy.[22] This muscle atrophy contributed to the development of sarcopenia. The secretion of leptin can be increased by Il-6 through its action on adipose.[23] IL-6 can disrupt protein synthesis and participate directly in protein decomposition, which then lead to the reduction of muscle mass.[24] Furthermore, IL-6 can increase adipose tissue lipolysis and promote hepatic gluconeogenesis and hepatic insulin resistance.[23] The reduction of muscle mass and strength is also association in the condition with increased level of TNF-α.[24] TNF-α can decrease myoD and myogenin expression via nuclear factor-kappa B (NF-kB) activation and impairment of the IGF-1 signaling pathway in skeletal muscle tissue. The decrease of myoD and myogenin expression will then inhibit the myoblast differentiation.[25] In particular, insulin resistance also contributes to sarcopenia through its effects on muscle fibers through the decreased protein synthesis and on muscle contraction through its decreased calcium intake [24] (Figure 1).

The decrease in anti-inflammatory mediators contributes to sarcopenia through various mechanisms. By oxidating fatty acid and translocating AMPK-stimulated GLUT4, adiponectin may regulate skeletal muscle. In addition, as age increased, adiponectin can promote or preserve muscle through the process of myogenesis in its satellite cells and the inhibition of proteolysis.[25-27] By inducing the activation of PI3K/AKT, increasing the expression and translocation of GLUT4, and promoting insulin-stimulated glucose uptake in older human myotubes in muscle fibers, Vaspin can promote insulin sensitivity during metabolic stress. Therefore the decrease in these mediators contributes to Sarcopenia [28] (Figure 1).

Skeletal muscle can influence adipose tissue through its myokines, such as myostatin and irisin. By reducing muscle protein synthesis and glucose uptake, myostatin can increase muscle atrophy. Beside this, irisin can reduce the muscle atrophy by facilitating the browning or 'beiging' of white adipose tissue, which then can promote the increase of subcutaneous fat.[26] Study in mice has shown that irisin injections can induce muscle hypertrophy through the synthesis of Akt/mTOR stimulated muscle protein. In particular, a lower circulating irisin concentration was found in postmenopausal women who presented with sarcopenia compared with women who were not having sarcopenia [29] (Figure 1).

Exercise and nutritional interventions have been found as potential approaches to alleviate the effect of sarcopenia. Resistance exercise training alone, or in combination with aerobic exercise training can promote the reduction of myostatin and the increase of irisin serum concentrations. Through the decrease in myostatin and the increase in irisin, exercise can maintain or improve muscle mass and strength [26] and promote the beiging process of white adipose tissue (WAT).[30] By increase the rate or level of plasma membrane receptor expression, exercise interventions may also improve muscle tissue sensitivity to leptin and adiponectin.[26] Therefore, exercise can be used to counteract the effect of the ageing process on subcutaneous fat and to promote muscle protein synthesis (Figure 1).

A meta-analysis has shown that muscle mass can be significantly improved by using several nutritional intervention, such as amino acids (AAs), creatine (CR), b-hydroxy-b-methylbutyrate (HMB), and protein with amino acids supplementation.[31] By acting as primary stimuli for muscle protein anabolism, essential and nonessential AAs can activate a protein complex influencing the metabolic response to nutrients and proteins called rapamycin complex 1.[31] This activation can initiate messenger RNA translation and improve muscle mass.[31] Even though the underlying mechanisms were still unknown, muscular hypertrophy can also being promoted by using the combination of CR supplementation and exercise.[31] By activating the mechanistic target of rapamycin, the use of HMB can decrease protein breakdown in skeletal muscle and its upregulation of protein synthesis [31] (Figure 1).

This study is not without limitations. First, only a few risk factors were examined in this matched case-control study. It is to be hoped that further studies will examine more risk factors, such as insulin resistance and nutrition status. Secondly, our study may have underestimated the prevalence of sarcopenia since we have excluded aged females with severe comorbidities who cannot perform assessments needed to diagnose sarcopenia in this study.

In conclusion, our study found that body mass index is not a risk factor for sarcopenia among elderly women. An interesting finding in this study is that the low percentage of whole-body subcutaneous fat is a potent risk factor of sarcopenia. This finding has supported the cross-talk hypothesis between fat tissue and muscle. Exercise and nutrition supplementation can be used to counteract the effect of the ageing process on subcutaneous fat and to promote muscle protein synthesis.

REFERENCE

1. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age and Ageing. 2019;48(4):601-.
2. Janssen I, Heymsfield SB, Ross R. Low Relative Skeletal Muscle Mass (Sarcopenia) in Older Persons Is Associated with Functional Impairment and Physical Disability. Journal of the American Geriatrics Society. 2002;50(5):889-96.
3. Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff R. The Healthcare Costs of Sarcopenia in the United States. Journal of the American Geriatrics Society. 2004;52(1):80-5.
4. Cruz-Jentoft AJ, Landi F, Schneider SM, Zúñiga C, Arai H, Boirie Y, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age and Ageing. 2014;43(6):748-59.
5. Volpato S, Bianchi L, Cherubini A, Landi F, Maggio M, Savino E, et al. Prevalence and clinical correlates of sarcopenia in community-dwelling older people: application of the EWGSOP definition and diagnostic algorithm. The journals of gerontology Series A, Biological sciences and medical sciences. 2014;69(4):438-46.
6. Aryana IS, Kuswardhani RT. Sarcopenia in Elderly. International Journal of Geriatrics and Gerontology. 2018;2018.(1)
7. Yamada M, Nishiguchi S, Fukutani N, Tanigawa T, Yukutake T, Kayama H, et al. Prevalence of sarcopenia in community-dwelling Japanese older adults. J Am Med Dir Assoc. 2013;14(12):911-5.
8. Statistics Indonesia [BPS]. Statistics on Elderly People 2017 (Statistik Penduduk Lanjut Usia 2017): Badan Pusat Statistik; Available from: https://www.bps.go.id/publication/download.html?nrbvfeve=N2ExMzBhMjJhYTI5Y2M4MjE5YzVkMTUz&xzmn=aHR0cHM6Ly93d3cuYnBzLmdvLmlkL3B1YmxpY2F0aW9uLzIwMTgvMDQvMTMvN2ExMzBhMjJhYTI5Y2M4MjE5YzVkMTUzL3N0YXRpc3Rpay1wZW5kdWR1ay1sYW5qdXQtdXNpYS0yMDE3Lmh0bWw%3D&twoadfnoarfeauf=MjAyMC0wNS0yMSAyMjowMzowNg%3D%3D.
9. Yu SCY, Khow KSF, Jadczak AD, Visvanathan R. Clinical Screening Tools for Sarcopenia and Its Management. Current Gerontology and Geriatrics Research. 2016;2016:10.
10. Bhasin S, Travison TG, Manini TM, Patel S, Pencina KM, Fielding RA, et al. Sarcopenia Definition: The Position Statements of the Sarcopenia Definition and Outcomes Consortium. Journal of the American Geriatrics Society. 2020;n/a(n/a).
11. Liguori I, Russo G, Aran L, Bulli G, Curcio F, Della-Morte D, et al. Sarcopenia: assessment of disease burden and strategies to improve outcomes. Clinical Interventions in Aging. 2018;13:913-27.
12. Unger T, Borghi C, Charchar F, Khan NA, Poulter NR, Prabhakaran D, et al. 2020 International Society of Hypertension Global Hypertension Practice Guidelines. Hypertension. 2020;75(6):1334-57.
13. World Health Organization (WHO). BMI classification: World Health Organization; 2006 [updated 12 August 2016; cited 2016 12 August]. Available from: http://apps.who.int/bmi/index.jsp?introPage=intro_html.
14. Chumlea WC, Guo SS, Kuczmarski RJ, Flegal KM, Johnson CL, Heymsfield SB, et al. Body composition estimates from NHANES III bioelectrical impedance data. International Journal of Obesity. 2002;26(12):1596-609.
15. Janssen I, Baumgartner RN, Ross R, Rosenberg IH, Roubenoff R. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. Am J Epidemiol. 2004;159(4):413-21.

16. Tasar PT, Sahin S, Karaman E, Ulusoy MG, Duman S, Berdeli A, et al. Prevalence and risk factors of sarcopenia in elderly nursing home residents. European Geriatric Medicine. 2015;6(3):214-9.
17. Lau EM, Lynn HS, Woo JW, Kwok TC, Melton LJ, 3rd. Prevalence of and risk factors for sarcopenia in elderly Chinese men and women. J Gerontol A Biol Sci Med Sci. 2005;60(2):213-6.
18. Sazlina S-G, Lee PY, Chan YM, A. Hamid MS, Tan NC. The prevalence and factors associated with sarcopenia among community living elderly with type 2 diabetes mellitus in primary care clinics in Malaysia. PLOS ONE. 2020;15(5):e0233299.
19. Palmer AK, Kirkland JL. Aging and adipose tissue: potential interventions for diabetes and regenerative medicine. Exp Gerontol. 2016;86:97-105.
20. Rogers NH, Landa A, Park S, Smith RG. Aging leads to a programmed loss of brown adipocytes in murine subcutaneous white adipose tissue. Aging Cell. 2012;11(6):1074-83.
21. Caso G, McNurlan MA, Mileva I, Zemlyak A, Mynarcik DC, Gelato MC. Peripheral fat loss and decline in adipogenesis in older humans. Metabolism: clinical and experimental. 2013;62(3):337-40.
22. Tazawa R, Uchida K, Fujimaki H, Miyagi M, Inoue G, Sekiguchi H, et al. Elevated leptin levels induce inflammation through IL-6 in skeletal muscle of aged female rats. BMC musculoskeletal disorders [Internet]. 2019 2019/05//; 20(1):[199 p.]. Available from: http://europepmc.org/abstract/MED/31077169
23. Han MS, White A, Perry RJ, Camporez J-P, Hidalgo J, Shulman GI, et al. Regulation of adipose tissue inflammation by interleukin Proceedings of the National Academy of Sciences. 2020;117(6):2751.
24. Bian AL, Hu HY, Rong YD, Wang J, Wang JX, Zhou XZ. A study on relationship between elderly sarcopenia and inflammatory factors IL-6 and TNF-α. Eur J Med Res. 2017;22(1):25.
25. Li F, Li Y, Duan Y, Hu CA, Tang Y, Yin Y. Myokines and adipokines: Involvement in the crosstalk between skeletal muscle and adipose tissue. Cytokine Growth Factor Rev. 2017;33:73-82.
26. Paris MT, Bell KE, Mourtzakis M. Myokines and adipokines in sarcopenia: understanding cross-talk between skeletal muscle and adipose tissue and the role of exercise. Current Opinion in Pharmacology. 2020;52:61-6.
27. De Carvalho FG, Justice JN, Freitas ECd, Kershaw EE, Sparks LM. Adipose Tissue Quality in Aging: How Structural and Functional Aspects of Adipose Tissue Impact Skeletal Muscle Quality. Nutrients. 2019;11(11):2553.
28. Thomas N, Chris C, Kostas T, Robert J, Leigh B, Edward TD, et al. Vaspin promotes insulin sensitivity in elderly muscle and is upregulated in obesity. Journal of Endocrinology. 2019;241(1):31-43.
29. Park H-S, Kim HC, Zhang D, Yeom H, Lim S-K. The novel myokine irisin: clinical implications and potential role as a biomarker for sarcopenia in postmenopausal women. Endocrine. 2019;64(2):341-8.
30. Severinsen MCK, Schéele C, Pedersen BK. Exercise and browning of white adipose tissue – a translational perspective. Current Opinion in Pharmacology. 2020;52:18-24.
31. Martin-Cantero A, Reijnierse EM, Gill BMT, Maier AB. Factors influencing the efficacy of nutritional interventions on muscle mass in older adults: a systematic review and meta-analysis. Nutr Rev. 2021;79(3):315-30.