Original Article

The Relationship between Insulin Resistance and the Degree of Sarcopenia in Elderly Patients on Maintenance Hemodialysis

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Abstract

Background: Sarcopenia is a condition that can decrease a person's quality of life and increase mortality in the elderly because it is often associated with cardiovascular complications. Insulin resistance is an important factor in the occurrence of sarcopenia. Old age and metabolic conditions such as chronic kidney disease on maintenance hemodialysis (MHD) can worsen insulin resistance, making sarcopenia prone to occur. There are few studies on the relationship between insulin resistance and the degree of sarcopenia in elderly patients on MHD. This study aimed at to analyze the relationship between insulin resistance and the degree of sarcopenia in elderly patients on MHD. **Method:** This study is an analytical observational study with a cross-sectional design in the elderly on MHD in Dr. Soetomo hospital Surabaya who met the inclusion criteria and did not meet the exclusion criteria. Examination of insulin resistance, using the HOMA IR formula and sarcopenia status adopting the 2019 AWGS standard. Data were analyzed using the Spearman correlation test. **Results:** From a total of 40 subjects, 70% severe sarcopenia, 12.5% sarcopenia, 5% presarcopenia, and 12.5% normal were found. The median value of HOMA IR is 2.29 (0.48-10.64). This study showed a positive correlation between insulin resistance and the degree of sarcopenia in elderly patients on MHD (p=0.001, r=0.496). In addition, there was also a significant relationship between HOMA IR and muscle mass (p<0.001) but not with muscle strength and physical performance (p=0,311; p=0,165). **Conclusion:** There is a relationship between insulin resistance and the degree of sarcopenia in elderly patients on MHD. The higher the HOMA IR, the more severe is the degree of sarcopenia. In addition, the relationship between insulin resistance and muscle mass was also found, but not on muscle strength and physical performance.

Keywords: Sarcopenia, Hemodialysis, Insulin Resistance, Elderly

Introduction

Sarcopenia is known as a geriatric syndrome characterized by a decrease in muscle mass with overall and progressive muscle strength and/or physical performance as a result of changes in muscle structure and function that can reduce the quality of life and increase mortality in the elderly.[1,2] The prevalence of sarcopenia in Asia is around 4.1%-16.3% in women and 5.5%-25.7% in men.[2] The etiology of sarcopenia is multifactorial in which insulin resistance is included and is also a result of the aging process.

Several studies have shown that insulin resistance can be an important factor in the occurrence of sarcopenia in patients on maintenance hemodialysis (MHD).[3-5] Insulin resistance mainly occurs in peripheral tissues

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and has occurred since the early stages of CKD. The mechanism of insulin resistance in CKD causing sarcopenia is thought to be due to impaired insulin signaling pathway on insulin receptor substrate (IRS)-1 associated phosphatidyl-inositol 3-kinase (PI3K) which is associated with chronic inflammation, metabolic acidosis, vitamin D deficiency, secondary hyperparathyroidism, uremic toxins, malnutrition, anemia, and adipokines.[6,7] The hemodialysis process itself can increase muscle protein degradation.[8] However, dialysis therapy also has a positive effect in reducing insulin resistance.[9]

Based on the data and information given above, insulin resistance is one of the important causes of decreased muscle mass and strength as a component of sarcopenia. In Indonesia, especially Surabaya, there has been no research on the relationship between insulin resistance and the degree of sarcopenia in elderly patients on MHD. Therefore, the researcher intends to analyze the relationship between insulin resistance with a degree of sarcopenia in elderly patients on MHD at the Hemodialysis Installation of Dr. Soetomo Hospital. It is hoped that this study will provide an overview of the characteristics of elderly patients on MHD concerning insulin resistance and the degree of sarcopenia, so that patient management can be done more comprehensively. With the formulation of the problem "Is there a relationship of insulin resistance with the degree of sarcopenia of elderly patients on MHD at the Hemodialysis Installation of dr. Soetomo Hospital".

Research Methods

The design of this study is an observational analytic with a cross-sectional study to determine the relationship between insulin resistance and the degree of Sarcopenia in elderly patients on MHD at the Hemodialysis Installation of dr. Soetomo Hospital Surabaya in the period from December 2020 to January 2021. The scope of the population is the entire patient population aged ≥60 years old who underwent continuous hemodialysis at the Hemodialysis Installation of dr. Soetomo Hospital Surabaya, who met the inclusion criteria and did not meet the exclusion criteria. The total samples obtained were 40 patients. The inclusion criteria of this study include:

1. Patient aged ≥60 years old who undergo hemodialysis for at least 3 months at the Hemodialysis Installation of Dr. Soetomo Hospital Surabaya.
2. Can communicate actively.
3. Ready to participate in the study and sign an informed consent form.

Exclusion criteria for this study include:

1. Acute infectious disease (clinical fever with suspected source of infection for less than 2 weeks)
2. Unable to understand examination instructions (severe functional impairment with ADL score ≤8 and severe cognitive impairment with MMSE score ≤18).
3. DM patients in therapy.
4. Patients with liver cirrhosis.
5. Patients with malignant disease.
6. Patients taking corticosteroid drugs, oral contraceptives, antipsychotics, protease inhibitors (PI) anti-retrovirals.
7. Patients with obesity.

Measurement of insulin resistance

Measurement of insulin resistance in this study used the HOMA IR formula.

HOMA-IR Formula = (Fasting Insulin x Fasting Blood Sugar) / 405

- Fasting insulin (mU/L) by ECLIA method.
- Fasting blood sugar (mg/dL) by colorimetric enzymatic method.

Measurement of muscle mass

Measurement of muscle mass obtained by ASM divided by height squared. ASM was obtained from the percentage of muscle mass in the upper and lower extremities measured using the Omron Karada Scan brand bioimpedance analysis model HBF 362.

The cut off value of low skeletal muscle mass using the 2019 AWGS standard is <7 kg/m^2 in men and <5.7 kg/m^2 in women using BIA.

Measurement of muscle strength

Measurement of muscle strength using handgrip strength which was measured 3 times using Dynamometer TKK 5001 Grip A and the highest was taken. Data collection is done with a distance of 30 seconds. The subject is prepared to stand and grip the dynamometer with the dominant hand and the arm should not be bent. The cut off value of low handgrip muscle strength using the 2019 AWGS standard, which is <28 kg for men and <18 kg for women.

Physical performance measurement

Measurement of physical performance by measuring the speed of walking at a distance of 6 meters divided by the travel time. The measurement method is that the inspection distance is calculated with a meter and marked with a measuring tape. Running time is calculated with a stopwatch. The cut-off value of low physical performance using the 2019 AWGS standard is <1.0 m/sec.

This research has been declared ethically worthy. All data were processed computerized using the IBM SPSS Statistics 25.0 program. Normality test with Shapiro-wilk. The basic characteristics of research subjects are

presented descriptively; numerical data is presented in the mean and standard deviation (normal distribution); in median and range (non-normal distribution) while categorical data are presented in frequency and percentage. chi-square test (categorical), t-test (numeric and normal distribution), and Mann-Whitney (numeric and abnormal distribution) were performed to compare groups. The type of data is ratio and nominal for insulin resistance and ordinal for the degree of sarcopenia. The relationship between variables was analyzed using the Spearman correlation test (numeric-ordinal). The interpretation of the correlation test results is based on the p-value, the strength of the correlation, and the direction of the correlation. Statistical analysis was declared significant if the p-value <0.05.

Research Result

In most of this study, the subjects were dominated by a group with an age range of 60-69 years with a total of 35 people (87.5%). The proportion of elderly men as many as 25 people (62.5%) and the remaining elderly women as many as 15 people (37.5%) from a total of 40 elderly people who were selected by total sampling and registered as continuous hemodialysis patients in the Hemodialysis Installation of Dr. Soetomo Hospital Surabaya has met the inclusion criteria and did not meet the exclusion criteria. The following is an analysis of the general characteristics of the research subjects presented descriptively.

Table 1. General sociodemographic profile of research subjects

Variable		Total N (%)
Age	Median (range)	64 (60-93)
Age range	60-69 years old	35 (87.5)
	70-79 years old	3 (7.5)
	≥80 years	2 (5)
Gender	Man	25 (62.5)
	Woman	15 (37.5)
Married status	Marry	32 (80)
	Widow/widower died	7 (17.5)
	Divorced widow/widower	0 (0)
	Not married yet	1 (2.5)
last education	Did not pass Elementary School	1 (2.5)
	Graduated from Elementary School	8 (20)
	Junior High School	10 (25)
	Senior High School / Vocational High School	12 (30)
	D3	1 (2.5%)
	Under Graduate (S1)	7 (17.5)
	Graduate (S2)	1 (2.5)
Income per month	<1.5 million	18 (45)
	1.5-3 million	14 (35)
	>3 million	8 (20)
Basic disease	Diabetes mellitus	22 (55)
	Hypertension	15 (37.5)
	Kidney stones	3 (7.5)

Table 2. Geriatric profile of research subjects

Variable		Total N (%)
BMI	Underweight	0 (0)
	Normal	33 (82.5)
	Overweight	7 (17.5)
	Obesity	0 (0)
MNA	Normal	8 (20)
	At risk of malnutrition	32 (80)
	Malnutrition	0 (0)
MMSE	Normal	31 (77.5)
	Mild cognitive impairment	9 (22.5)
	Severe cognitive impairment	0 (0)
ADL	Independent	26 (65)
	Mild dependency	11 (27.5)
	Moderate dependency	3 (7.5)
	Severe dependency	0 (0)
	Total dependency	0 (0)
GDS	Normal	29 (72.5)
	Possible depression	11 (27.5)
	Depression	0 (0)
PASE	Low	31 (77.5)
	Mild	9 (22.5)
	Moderate-intense	0 (0)

Table 3. Profile of the research subject's hemodialysis medical data

Variable		Total N (%)
Base data		
Length of HD	Median (range)	4 (0.5-21)
HD Frequency	1x a week	0 (0)
	2x a week	40 (100)
1x HD duration (hours)	Median (range)	4.5 (4-5)
HD duration a week (hours)	Median (range)	9 (8-10)
History of transfusion in the last 3 months	Yes	21 (52.5)
	Not	19 (47.5)
Received erythropoietin in the last 3 months	Yes	30 (75)
	Not	10 (25)
Hepatitis	No hepatitis	27 (67.5)
	Hepatitis B	7 (17.5)
	Hepatitis C	6 (15)
Physical examination data		
Systolic blood pressure	≤139 mmHg	17 (42.5)
	140-159 mmHg	19 (47.5)
	≥160 mmHg	4 (10)
BW before HD (kg)	Median (range)	64 (43.2-84.5)
BW after HD (kg)	Median (range)	61.3 (41.9-80.1)
Difference in weight (kg)	Median (range)	2.4 (0.1-5.3)
Ultrafiltration (liters)	Median (range)	2.55 (0-5)
Laboratory parameter data		
Hemoglobin (g/dl)	Median (range)	9.15 (5.9-13.4)
Transferrin saturation (%)	Median (range)	30.9 (12.66-86.96)
BUN (mg/dl)	Median (range)	71 (26-105)
Serum creatinine (mg/dl)	Median (range)	12.2 (4.4-17.4)
Albumin (g/dl)	Median (range)	3.39 (2.76-3.8)
Calcium (mg/dl)	Median (range)	8.75 (6.7-10.5)
Phosphate (mg/dl)	Median (range)	5.7 (2.4-9.7)
Uric acid	Median (range)	7.1 (3-11.3)

Profile of study subjects on the degree of sarcopenia in elderly patients undergoing continuous hemodialysis

Based on the 2019 AWGS, this study found that out of a total of 40 patients, 70% had severe sarcopenia, 12.5% sarcopenia, 5% presarcopenia, and 12.5% normal. The number of subjects with low total muscle mass was 87.5% compared to normal muscle mass. From the total 87.5%, low muscle mass suffered the most in the severe sarcopenia group, which was 70%, the others were 12.5% sarcopenia and 5% presarcopenia. Research subjects with the low handgrip strength of 87.5% compared to normal only 12.5%. From a total of 87.5%, low handgrip strength suffered the most in the severe sarcopenia group 70%, others 5% sarcopenia, and 12.5% normal. Research subjects with a low physical performance by 90% compared to normal only 10%. From the total 90%, Low physical performance suffered the most in the 70% severe sarcopenia group, the other 7.5% sarcopenia and 12.5% normal. In this study, the normal and presarcopenia groups were combined into a non-sarcopenia group because the number of presarcopenia was only 2 people, so that with this combination the normality test could only be assessed.

Table 4. Data analysis of research subject profiles at various degrees of sarcopenia

Variable		Degree of Sarcopenia				
		Non Sarcopenia N=7	Sarcopenia N=5	Severe Sarcopenia N=28	p value	r
Profile based on sociodemographic variables						
Gender	Men, N (%)	6 (85.7)	4 (80)	15 (53.6)	0.200	0.273
	Woman, N (%)	1 (14.3)	1 (20)	13 (46.4)		
Age range	60-69 years, N (%)	7 (100)	5 (100)	q	0.131	0.243
	70-79 years, N (%)	0 (0)	0 (0)	3 (10.7)		
	≥ 80 years, N (%)	0 (0)	0 (0)	2 (7.1)		
Basic disease	Diabetes, N (%)	3 (42.9)	1 (20)	18 (64.3)	0.258	0.342
	Hypertension, N (%)	4 (57.1)	3 (60)	8 (28.6)		
	Kidney stones, N (%)	0 (0)	1 (20)	2 (7.1)		
Profile based on geriatric variables						
Upper arm circumference (cm)	Mean+ sd	25.8+2.82	26.1+3.21	23.4+3.92	0.032	-0.339
Calf circumference (cm)	Mean+ sd	32.5+1.75	33.1+3.32	29.5+3.47	0.002	-0.476
MNA	Normal, N (%)	5 (71.4)	0 (0)	3 (10.7)	0.005	0.433
	At risk of malnutrition, N (%)	2 (28.6)	5 (100)	25 (89.3)		
MMSE	Normal, N (%)	6 (85.7)	4 (80)	21 (75)	0.554	0.096
	Mild cognitive impairment, N (%)	1 (14.3)	1 (20)	7 (25)		
ADL	Independent, N (%)	6 (85.7)	3 (60)	17 (60.7)	0.263	0.181
	Mild dependence, N (%)	1 (14.3)	2 (40)	8 (28.6)		
	Moderate dependency, N(%)	0 (0)	0 (0)	3 (10.7)		
PASE	Mild, N (%)	7 (100)	2 (40)	0(0)	<0.001	0.878
	Low, N (%)	0(0)	3 (60)	28 (100)		
Profile based on hemodialysis variables						
HD duration (years)	Median (range)	5(1.5-8)	4(2-9)	3(0,5-21)	0.193	-0.210
HD duration in 1 week (hours)	Median (range)	9(8-9.5)	9(9-10)	9(8-10)	0.607	0.084
Hepatitis	No hepatitis, N (%)	4 (57.1)	3 (60)	20 (71.4)	0.305	0.328
	Hepatitis B, N (%)	3 (42.9)	1 (20)	3 (10.7)		
	Hepatitis C, N (%)	0 (0)	1 (20)	5 (17.9)		
Hemoglobin (g/dl)	Mean+ sd	11.9+1.09	10.3+1.38	8.7+1.25	<0.001	-0.653
BUN (mg/dl)	Mean+ sd	72+23.27	69.4+22.42	68.6+23.31	0.880	-0.025
Albumin (g/dl)	Mean+ sd	3.45+0.17	3.43+0.27	3.30+0.28	0.115	-0.253
Calcium (mg/dl)	Median (range)	9.1(8,2-10)	8.5(8.1-9)	8.8(6.7-10.5)	0.973	0.006
Phosphate (mg/dl)	Mean+ sd	6.8+1.61	6.6+1.95	5.3+1.81	0.019	-0.370

HOMA IR profile in the elderly undergoing continuous hemodialysis

This study found the median value of HOMA IR was 2.29 with the lowest value of 0.48 and the highest value of 10.64. The reference range for the normal value of HOMA IR in this research subject is <1.56 based on the 2015 study by Akalin et al. in MHD.[9] In the research subjects, 31 people (77.5%) had high HOMA IR while 9 people (22.5%) had normal HOMA IR.

Table 5. Data analysis of research subject profiles based on HOMA IR

Variable		HOMA IR		p value
		Normal N=9	High N=31	
Profile based on sociodemographic variables				
Gender	Men, N (%)	7 (77.8)	18 (58.1)	0.440
	Woman, N (%)	2 (22.2)	13 (41.9)	
Age range	60-69 years, N (%)	8 (88.9)	27 (87.1)	
	70-79 years, N (%)	0 (0)	3 (9.7)	0.419
	≥ 80 years, N (%)	1 (11,1)	1 (3,2)	
Underlying disease	Diabetes Mellitus, N (%	5(55,6)	17 (54.8)	0.600
	Hypertension, N (%)	4 (44.4)	11 (35.5)	
	Kidney stones, N (%)	0 (0)	3 (9.7)	
Profile based on geriatric variables				
MNA	Normal, N (%)	5 (55.6)	3 (9.7)	
	At risk of malnutrition, N (%)	4 (44.4)	28 (90.3)	0.002
MMSE	Normal, N (%)	7 (77.8)	24 (77.4)	
	Mild cognitive impairment, N (%)	2 (22.2)	7 (22.6)	0.982
ADL	Independent, N (%)	7 (77.8)	19 (61.3)	
	Mild dependence, N(%)	1 (11,1)	10 (32,3)	0.443
	Moderate dependency, N(%)	1 (11,1)	2 (6.4)	
PASE	Mild, N (%)	1 (77.8)	8 (6.5)	<0.001
	Low, N (%)	8 (22.2)	23 (93.5)	
Profile based on hemodialysis variables				
HD duration (years)	Median (range)	4(1-8)	3.5(1-21)	0.961
HD duration in 1 week (hours)	Median (range)	9(8-9.5)	9(8-10)	0.723
Hepatitis	No hepatitis, N (%)	6 (66.7)	21 (67.7)	0.182
	Hepatitis B, N (%)	3 (33.3)	4 (12.9)	
	Hepatitis C, N (%)	0 (0)	6 (19.4)	
Hemoglobin (g/dl)	Mean+sd	10.9+2.17	9.09+1.34	0.003
BUN (mg/dl)	Mean+sd	69.9+25.03	69.1+22.34	0.931
Albumin (g/dl)	Mean+sd	3.5+0.15	3.3+0.28	0.139
Calcium (mg/dl)	Median (range)	9.1(8,2-10)	8.7(6.7-10.5)	0.399
Phosphate (mg/dl)	Mean+sd	6.3+1.76	5.5+1.89	0.325

The relationship between insulin resistance and the degree of sarcopenia in elderly patients undergoing continuous hemodialysis

Based on table 6, there was a positive correlation between HOMA IR status and the degree of sarcopenia which was significant (p=0.001, r=0.496) in the elderly on MHD at the Hemodialysis Installation of Dr. Soetomo Hospital.

Table 6. Correlation of the HOMA IR profile with the degree of sarcopenia

Variable	Total	Non sarkopenia	Sarcopenia	Severe Sarcopenia	Nilai p	r
HOMA IR	2,29 (0,48-10,64)	0,87 (0,48-1,48)	2,73 (1,85-3,07)	2,36 (1,44-10,64)	0,001	0,496

The relationship between the components of sarcopenia and HOMA IR status in the elderly undergoing continuous hemodialysis

The characteristics of the HOMA IR status profile on various components of sarcopenia, namely muscle mass, handgrip strength, and physical performance can also be seen in table 7. The table shows a relationship between muscle mass, and HOMA IR status (p<0.001). while the relationship between muscle strength, physical performance and HOMA IR status was not significant (p=0,311; p=0,165).

Table 7. Relationhip between sarcopenia component and HOMA IR status

Components of Sarcopenia		HOMA IR		p value
		Normal	High	
Muscle mass	Low, N (%)	4 (44.4)	31 (100)	<0.001
	Normal, N (%)	5 (55.6)	0 (0)	
Handgrip strength	Low, N (%)	7 (77.8)	28 (90.3)	0.311
	Normal, N (%)	2 (22.2)	3 (9.7)	
Physical performance	Low, N (%)	7 (77.8)	29 (93.5)	0.165
	Normal, N (%)	2 (22.2)	2 (6.5)	

Discussion

Profile of study subjects on the degree of sarcopenia in elderly patients undergoing continuous hemodialysis

Based on the 2019 AWGS, this study found that out of a total of 40 patients, 70% had severe sarcopenia and 12.5% only had sarcopenia. The rests were 5% presarcopenia and 12.5% normal. Based on research in China by Cheng *et al*.[10] with a larger number of samples, namely 238 patients, the average age was 60.9 years, those with severe sarcopenia were 30.7% and only sarcopenia was 49.2%. Lin *et al*.[11] showed the results of sarcopenia in patients aged >65 and <65 years about 65% and 35%, respectively.[11]

Based on table 4, men were more likely to experience sarcopenia and severe sarcopenia than women (80% vs 20%; 53.6% vs 46.4%), although not significant (p=0.200). Similar results in a study in South Korea by Kim *et al*.[12] showed 51.15 of men while 48.9% of women experienced sarcopenia in the elderly on MHD (p=0.311). Research in America by Kittiskulnam *et al*.[13] also showed that elderly men on MHD experienced greater sarcopenia, namely 61% than women.[13] This is probably due to a greater decrease in testosterone in men than in women and a significant decrease in IGF-1 resulting in a rapid decrease in muscle mass and strength. In women at the beginning of menopause, there is a decrease in body estrogen levels resulting in a decrease in muscle mass and function but also conversion from androgen hormones to estrogen in adipose tissue so that it can be a protective factor for sarcopenia.[14,15]

In this study, there was a negative correlation between the size of upper arm circumference and the degree of sarcopenia, with a weak correlation strength. The increasing size of upper arm circumference, the less sarcopenia (p=0.032, r=-0.339). In addition, this study also found a negative correlation between the size of calf circumference (CC) and the degree of sarcopenia with a moderate strength of the correlation. The greater the size of the CC, the less are the chances of sarcopenia (p=0.002, r=-0.476). Similarly, in a study in China by taking subjects from nursing homes aged >60 years, there was a significant negative correlation between upper arm circumference, CC, and sarcopenia with a weak correlation strength (upper arm circumference p=0.001, r=-0.192; CC p=0.000, r=-0.280).[16] Anthropometric measurements of upper arm circumference and CC can be used to indirectly determine muscle mass in predicting the risk of sarcopenia, however, it is still affected by the increase in body fat content and the decrease in skin elasticity during aging, and the correlation with sarcopenia may not be significant.[17]

In this study, subjects with MNA results at risk of malnutrition dominated in the severe sarcopenia group of 89.3% and 100% sarcopenia. The results also showed a positive correlation between malnutrition and the degree of sarcopenia, which was significant with a moderate strength of the correlation. The more nutritional disorders occur, the more severe the degree of sarcopenia (p=0.005, r=0.433). Research carried out in Japan by Sakai *et al*.[18] showed a significant relationship between malnutrition and sarcopenia in elderly patients in rehabilitation hospitals (p < 0.002). This can be explained that a low intake of nutrients and protein results in a decrease in lean body mass and muscle wasting occurs, thus affecting muscle mass and muscle strength.[19]

Low PASE results predominated in the 100% severe sarcopenia and 60% sarcopenia groups. The results also showed a positive correlation between PASE and the degree of sarcopenia, which was significant with a strong correlation. The lower the activity, the more severe the degree of sarcopenia (p=0.000, r=0.878). This can be explained based on the theory that low physical activity will reduce muscle strength, before a decrease in muscle mass results in a decrease in functional capacity.[20] Interventions in the form of resistance exercise can induce muscle hypertrophy and increase muscle strength in the elderly.[21]

This study also found a significant negative correlation between hemoglobin levels and the degree of sarcopenia with a moderate strength of correlation (p < 0.001, r=-0.653). This is similar to the study in the community aged >65 years by Vogrin *et al*.[22] there was a significant difference in hemoglobin levels between the sarcopenia and non-sarcopenia groups (p=0.001). Research by Kim *et al*.[12] showed that there was no significant difference in hemoglobin levels between the sarcopenia and non-sarcopenia groups in patients on MHD (p=0.099). This may be because in this study the sample was taken from >60 years of age while Kim *et al*.[12] from age >18 years. Anemia can affect a decrease in muscle strength and mass due to a decrease in oxygen transport to tissues, resulting in hypoxia which results in easy fatigue and muscle weakness. Anemia also indirectly increases inflammatory cytokines.[23]

A negative correlation was found between phosphate levels and the degree of sarcopenia with a weak correlation strength (p=0.019, r=-0.370). The lowest phosphate levels were found in the severe sarcopenia group, followed by sarcopenia. Loss of appetite due to anorexia often occurs in patients on MHD due to uremic conditions while the main source of phosphate comes from a high protein diet so that phosphate levels in the body will decrease.[24]

HOMA IR Profile in Elderly Undergoing Continuous Hemodialysis

In this study, nutritional status (MNA) had a significant difference between normal and high HOMA IR status. The proportion of patients in the malnutrition risk group with high HOMA IR was 90.3%. Subjects at risk of malnutrition had a tendency to develop insulin resistance (p=0.002). Holvoet *et al*.[25] reported that the elderly on MHD are at risk of experiencing malnutrition by 59.3%.[24] Poor nutritional conditions can affect insulin resistance due to receptor and post-receptor defects which result in decreased affinity for insulin.[26]

This study also showed that there was a significant difference between PASE status with normal and high HOMA IR (p<0.001). Low PASE has a high HOMA IR proportion of 93.5%. Logan *et al*.[27] showed that the correlation between PASE scores and HOMA IR status was not significant in the community aged >60 years in Canada (p=0.208) and was negatively correlated. [26] Inactive skeletal muscle will trigger the tissue to develop an insulin resistance.[28] Several previous studies in adults have shown that aerobic or resistance exercise can improve glycemic regulation and increase insulin sensitivity. This is associated with an increased translocation of GLUT4 into the cell membrane so that glucose uptake also increases.[29]

This study found a significant difference in hemoglobin levels with normal and high HOMA IR (p=0.003). Research by Sit *et al*.[30] showed a significant difference in the mean hematocrit between normal and high HOMA IR status in patients on MHD (p<0.05). [29] Low hemoglobin levels indirectly affect insulin resistance through inflammatory pathways because low hemoglobin can increase inflammatory cytokines. [23,30]

The relationship between insulin resistance and the degree of sarcopenia in elderly patients undergoing continuous hemodialysis

Based on table 6, there was a positive correlation between HOMA IR status and the degree of sarcopenia, which was significant in the elderly on MHD (p=0.001, r=0.496). The research of Siew *et al*.[31] showed a significant positive correlation between insulin resistance and muscle protein breakdown in non-diabetic >45 years of age undergoing hemodialysis (p=0.001, R^2=0.49). Jeong *et al*.[32] showed that there was a significant difference between HOMA IR and the degree of sarcopenia undergoing continuous hemodialysis (p=0.041), and the median value of insulin resistance was the highest in the sarcopenia group.[31] Insulin resistance is an important factor in the occurrence of sarcopenia because it has a role in increasing protein degradation and decreasing muscle protein synthesis through inhibition of the IRS tyrosine phosphorylation pathway [33].

The relationship between the components of sarcopenia and insulin resistance in the elderly undergoing continuous hemodialysis

In this study, an analysis of the relationship between HOMA IR status and sarcopenia component was conducted using the Fisher test. Based on table 7, there was a relationship between muscle mass and HOMA IR status (p<0.001). Low muscle mass dominated 100% in the high HOMA IR group. Chao *et al*.[34] showed a significant association between muscle mass and HOMA IR (p<0.05) in the elderly community in Taiwan. Jeong *et al*.[32] showed that muscle mass had a negative correlation with HOMA IR in patients on MHD (p=0.015, r=-0.202). Resistance and endurance exercise can increase muscle mass and increase insulin sensitivity. This is associated with preventing mitochondrial dysfunction and increasing GLUT4 translocation into cell membranes.[35] In addition, the inhibitory role of skeletal muscle myostatin can increase muscle mass and glucose uptake by increasing GLUT1/GLUT4.[36].

There was no significant correlation between handgrip strength and physical performance with HOMA IR status (p=0.311; p=0.165). However, it can be seen that low handgrip strength dominates by 90.3% in high HOMA IR. Park *et al*.[37] also showed a non-significant negative correlation between handgrip strength, SPPB score and HOMA IR in a community of women aged >60 years in Korea (p=0.683, r=-0.032; p=0.467, r=-0.083). Li *et al*.[38] the results showed that hand-grip strength and HOMA IR had a significant relationship (p=0.025). Inflammation, impaired muscle oxidative capacity, and fat infiltration in muscle are important factors in the development of insulin resistance and are often associated with low muscle strength. Low GLUT4 in muscle cell membranes can also occur in people with low muscle strength.[38]

Conclusion and Suggestion

Conclusion

The research subjects were dominated by the 60-69 year age group, male, at risk of malnutrition, and had a median value of having undergone hemodialysis for 4 years with a duration of hemodialysis in a week for 9 hours. This study found that the number of subjects with severe sarcopenia was 70%, sarcopenia 12.5%, presarcopenia 5%, and normal 12.5% based on the 2019 AWGS.

Median value of HOMA IR in this study was 2,29. High HOMA IR status suffered by many subjects who were more at risk of malnutrition, low activity, and anemia. High HOMA IR status was dominated by subjects

who had low muscle mass, hand grip strength, and physical performance. This study shows that there is a relationship between insulin resistance and the degree of sarcopenia, where the higher the HOMA IR value, the more severe the degree of sarcopenia.

Suggestion

There is a need for a study with a cohort design to determine the role of insulin resistance on the degree of sarcopenia with a larger number of samples in the elderly on MHD and tight control of various factors that affect the degree of sarcopenia and use the gold standard test for insulin measurement.

Limitations and weaknesses

1. This study was a cross-sectional study which was carried out at a certain time so that it could not describe the course of the patient's condition until the HOMA IR was high.
2. Confounding factors that cannot be fully controlled such as hypertension, diabetes mellitus, anemia, previous food intake, and physical activity carried out by research subjects due to limitations of research implementation and research subjects, so that they can affect the relationship between insulin resistance and the degree of sarcopenia.

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