Original article

Neutrophil-to-lymphocyte ratio is not associated with muscle mass, strength, and functional capacity in hemodialysis patients

Razão de neutrófilo para linfócito não é associada à massa muscular, força e capacidade funcional em pacientes em hemodiálise

DOI: 10.37111/braspenj.2023.38.4.11

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ABSTRACT

Introduction: The association of neutrophil-to-lymphocyte ratio (NLR) with muscle mass, strength, and functional capacity was evaluated in hemodialysis (HD) patients. **Methods:** A cross-sectional study was performed evaluating 68 adults and older adults of both sexes undergoing HD. Bioelectrical impedance analysis (BIA) was used to obtain the appendicular skeletal muscle mass (ASMM). Handgrip strength (HGS) and 4 m-gait speed (GS) tests were performed to assess the muscle strength and functional capacity, respectively. The pollicis muscle thickness (APMT) was used as indicator of muscle mass. Multiple regression analyses were carried out to assess the association of NLR with ASMM, HGS, GS, and APMT, adjusting for confounders (age, sex, HD time, and smoking habit). **Results:** Out of 68 (59.1 ± 14.2y) HD patients evaluated, most were men (64.7%) and were overweight (BMI = 26.81 ± 4.8 kg/m²). After adjustments for confounders, NLR was not associated with ASMM (β: 0.029, p=0.66), HGS (β: -0.007, p=0.66), GS (β: -0.310, p=0.72) or APMT (β: -0.061, p=0.14). **Conclusion:** NLR is not associated with muscle mass, strength, and functional capacity in HD patients.

Keywords:
Hemodialysis. Neutrophil. Lymphocyte. Muscle mass. Muscle function.

Unitermos:
Hemodiálise. Neutrófilo. Linfócito. Massa muscular. Função muscular.

RESUMO

Introdução: A associação da razão de neutrófilos e linfócitos (RNL) com a massa, força e capacidade funcional muscular foi avaliada em pacientes em hemodiálise (HD). **Método:** Um estudo transversal foi feito, avaliando 68 adultos e adultos mais velhos, dos dois sexos, sob HD. A análise de impedância bioelétrica (BIA) foi utilizada para obter a massa muscular esquelética apendicular (MMEA). Teste de força de preensão manual (FPM) e velocidade de marcha em 4 metros (VM) foram utilizados para observar a força muscular capacidade funcional, respectivamente. A espessura do músculo adutor do polegar (EMAP) foi utilizada como um indicador da massa muscular. Análises de regressão múltipla foram feitas para investigar a associação entre RNL e MMEA, FPM, VM e EMAP, ajustando para confundidores (idade, sexo, tempo de HD e hábito de fumar). **Resultados:** Dos 68 (59.1 ± 14.2 anos) pacientes de HD avaliados, a maioria eram homens (64.7%) e estavam acima do peso (BMI = 26.81 ± 4.8 kg/m²). Depois do ajuste para confundidores, a RNL não estava associada à MMEA (β: 0.029, p=0.66), FPM (β: -0.007, p=0.66), VM (β: -0.310, p=0.72) ou EMAP (β: -0.061, p=0.14). **Conclusão:** A RNL não está associada à massa, força ou capacidade funcional muscular em pacientes em HD.

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Submission:
October 10, 2023

Accepted for publication:
December 8, 2023

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INTRODUCTION

The prevalence of sarcopenia in hemodialysis (HD) patients is of around 31.5%[1], which seems to be associated with increased levels of pro-inflammatory cytokines such as interleukin 6 (IL 6), Tumor Necrosis Factor-alpha (TNF-alpha) and C-reactive protein (CRP). However, due to the high cost to measure these inflammatory markers, a simple and low-cost inflammatory indicator that has been used is the neutrophil-lymphocyte ratio (NLR), obtained by dividing the total neutrophil count by the lymphocyte count[2].

Although NLR has been mainly used as a prognostic factor in cardiovascular mortality, cancer and for predicting worsening renal function in patients with diabetes, its use in dialysis patients is still unclear, requiring further studies to determine if NLR values are associated with muscle mass and strength in this population[2]. Thus, we hypothesized that a high NLR value would be associated with low muscle mass, strength, and function. Therefore, the present study sought to evaluate the association of NLR with muscle mass, strength, and functional capacity in HD patients.

METHODS

The cross-sectional study was performed during 2019, between the months of August and December. Adult patients of both sexes with chronic kidney disease (CKD) undergoing hemodialysis (HD) treatment for over 3 months were included in the sample. The study was carried out on site in a private HD clinic in Goiania, Brazil. From 119 patients enrolled, 51 were excluded from the study, and the final sample was composed of 68 (64.7% men) patients (Figure 1). All patients signed an Informed Consent Form, which was approved by the Ethical Committee of the Federal University of Goiás (protocol 3.384.866).

Clinical data were assessed through a specific questionnaire prepared by the researchers, with questions that could contribute to the analyses. The questions involved age, HD time, and practice of physical activity, smoking habit, alcohol intake, and use of oral nutritional supplements (ONS). Body weight and height were obtained using a balance scale and a portable stadiometer (SECA®, Hamburg, Germany), respectively. After the HD session, the bioelectrical impedance analysis (BIA) (Bodystat QuadScan 4000) was used to obtain the appendicular skeletal muscle mass (ASMM) value. The BIA evaluation was performed with the patient in the supine position, after the intermediate HD session (2nd session), to avoid interference from interdialytic weight gain. Eight disposable electrodes were used, in the positions of the wrists and between the malleolus of the hands, on the ankles and between the metatarsals of the feet. ASMM represents 73-75% of skeletal muscle mass (SMM). It was calculated

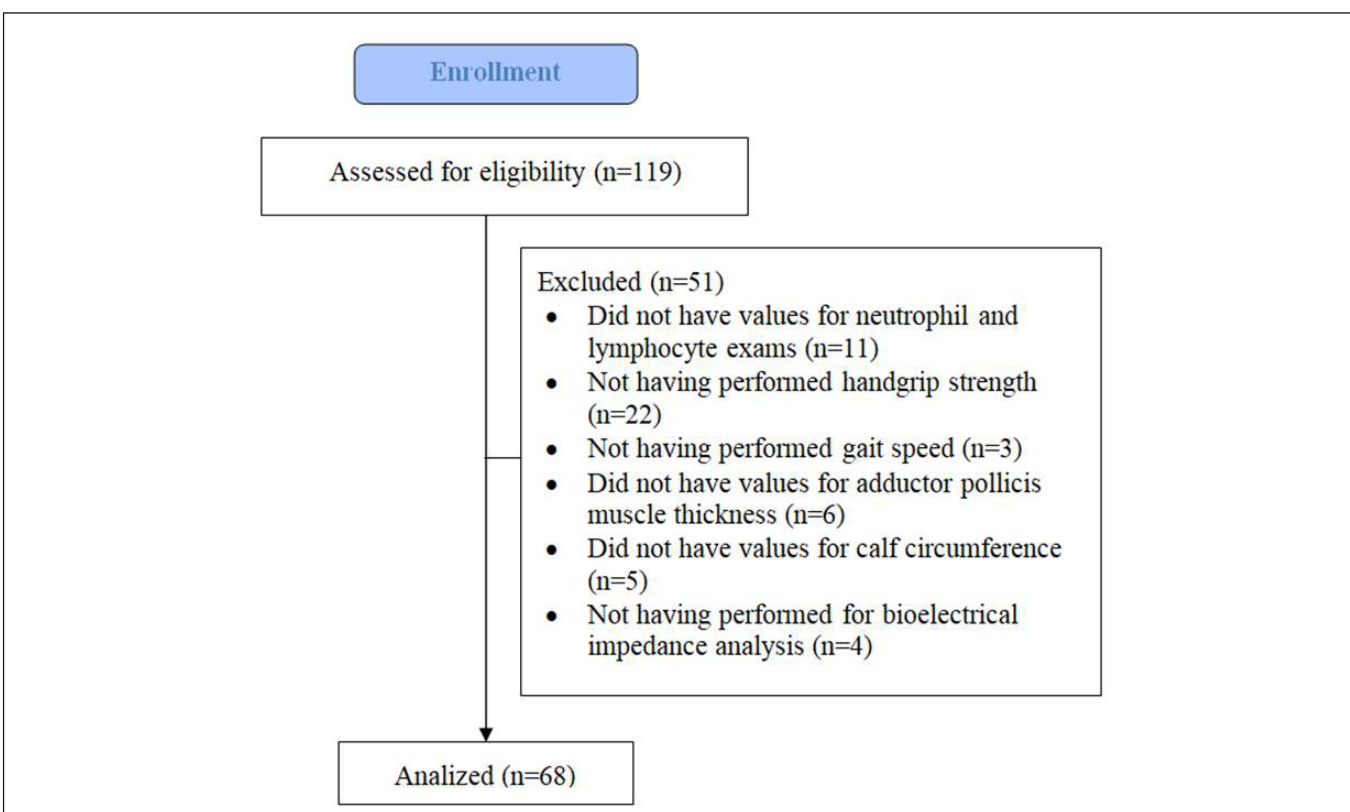

Figura 1 - *Selection of hemodialysis patients.*

from the formula where ASMM (kg) is equal to -3,964 + (0.227 * RI) + (0.095 * weight) + (1,384 * Sex) + (0.064 * Xc)[3], where RI is the resistive index (height^2/resistance), XC is the reactance (ohm), and the values for sex are 1 and 0 for men and women, respectively. The handgrip strength (HGS) was performed on the dominant hand, in the limb that did not have an arteriovenous fistula, using a portable digital dynamometer (Camry). The gait speed (GS) was performed with the volunteers walking in a straight line on an obstacle-free course for four meters and a speed below 0.8 m/s was considered low. The pollicis muscle thickness (APMT) and calf circumference (CC) were evaluated using a skinfold caliper (Cescorf, Porto Alegre, RS) and flexible tape, respectively. The results of netrophil and lymphocyte values were collected from the patients' medical records. These collections are carried out monthly by the institution and are analyzed in a third-party laboratory.

All data were analyzed using the Medcalc® (Belgium) and Statistical Package of Social Sciences (SPSS). To assess the difference between the tertiles of NLR, the ANOVA or Pearson's chi-square test were used. Descriptive statistics were used, such as absolute and relative frequencies, means and standard deviation. Linear regression analyses were carried out to assess the association of the NLR with ASMM, HGS, CC, GS, and APMT, using a crude model and adjusted for confounders (age, sex, HD time, and smoking habit). The level of statistical significance was established at 5%.

RESULTS

Out of the 68 (59.1±14.2y, ranging from 23 to 83 years old) HD patients evaluated, most were men (64.7%) and overweight (BMI = 26.81±4.8 kg/m^2). The characteristics of the patients of the study were divided into tertiles of NLR (Table 1). The patients were homogeneous among the tertiles of NLR regarding sex, age, BMI, HD time, physical activity, alcohol intake, smoking habit, use of ONS, lean and muscle mass, strength, and functional capacity.

Table 1 – Characterization of hemodialysis patients.

Variables	Tertile 1 n=24	Tertile 2 n=22	Tertile 3 n=22	p-value*
Neutrophil lymphocyte ratio	1.5 ± 0.4	2.4 ± 0.3	4.6 ± 1.9	0.01[a]
Sex, n (%)				
Female	8 (33.3)	11 (50.0)	5 (22.7)	0.16
Male	16 (66.7)	11 (50.0)	17 (77.3)	
Age (years)	56.3 ± 15.5	61.3 ± 14.3	59.9 ± 12.3	0.48[a]
Body mass index (kg/m2)	25.0 ± 4.5	27.9 ± 4.3	27.5 ± 5.2	0.08[a]
Hemodialysis diagnosis (years)	49.0 ± 21	50.0 ± 21.0	53.0 ± 16.0	0.80
Lean mass (kg)	46.1 ± 10.4	44.8 ± 10.0	51.2 ± 13.9	0.15[a]
ASMM (kg)	17.8 ± 3.5	18.0 ± 3.9	19.96 ± 5.74	0.43[a]
Gait speed (m/s)	0.8 ± 0.2	0.7 ± 0.2	0.6 ± 0.2	0.18[a]
Handgrip strength (kg)	29.4 ± 9.0	22.2 ± 10.7	25.7 ± 10.2	0.05[a]
Physical activity, n (%)				
Did not answer	1 (4.2)	-	2 (9.1)	
Practice	11 (45.8)	9 (40.9)	7 (31.8)	0.57[b]
No practice	12 (50)	13 (59.1)	13 (59.1)	
Smoking, n (%)				
Did not answer	1 (4.2)	-	2 (9.1)	
Smoker/ex-smoker	9 (37.5)	11 (50.0)	8 (36.4)	0.58[b]
No	14 (58.3)	11 (50.0)	12 (54.5)	
Alcoholism, n (%)				
Did not answer	1 (4.2)	-	2 (9.1)	
Yes	6 (25.0)	7 (31.8)	4 (18.2)	0.57[b]
No	17 (70.8)	15 (68.2)	16 (72.7)	
Nutritional supplementation, n (%)				
Did not answer	1 (4.2)	-	2 (9.1)	
Yes	1 (4.2)	1 (4.5)	4 (18.2)	0.19[b]
No	22 (91.6)	21 (95.5)	16 (72.7)	

[a]Pearson Chi-Square; [b]ANOVA; *p<0.05 was considered as significant.

In a multiple regression analysis, NLR was positively associated with ASMM and CC in crude analysis. However, these associations were no longer significant after adjustments for confounders. NLR was not associated with HGS, GS, and APMT in crude analyses and after adjustments for confounders (Table 2).

Table 2 – Linear regression analysis of NLR with muscle mass, strength, and functional capacity.

Variables	No adjustment		Adjusted	
	β	p-value*	β	p-value*
Appendicular skeletal muscle mass	0.17	< 0.01	0.02	0.66
Handgrip strength	0.05	0.94	-0.00	0.66
Calf circumference	0.85	<0.01	-0.00	0.91
Gait speed	-0.02	0.17	-0.31	0.72
Adductor pollicis muscle thickness	-0.56	0.05	-0.06	0.14

*p<0.05 was considered as significant.

DISCUSSION

NLR was not associated with muscle mass, strength, and functional capacity in HD patients, which is contrary to our initial hypothesis. Thus, despite some studies showing that NLR can be a marker of cardiovascular events and mortality in HD[4,5], our study was the first to investigate the association of NLR with strength and muscle mass in HD patients.

When considering conditions of low-grade inflammation, such as aging, NLR has been shown to be correlated with loss of lean mass, and is a possible predictor of sarcopenia[6,7]. Öztürk et al. (2018)[7] observed a negative correlation between lean mass and NLR in older adults with sarcopenia, but this association was not observed in individuals without sarcopenia. However, although there is some evidence that NLR can be associated with muscle mass in individuals without kidney diseases[7], the present study showed that NLR was not associated with muscle mass and its function in CKD patients, which can show that the association between NLR and muscle mass can be dependent on the type of population evaluated.

NLR has been associated with mortality and worse estimated glomerular filtration rate in CKD. Xin An et al. found a positive association between NLR and mortality by cardiovascular causes in Chinese patients performing peritoneal dialysis[8]. A study conducted in 350 patients with stage 1–4 CKD demonstrated that high NLR levels are associated with poor outcomes in the treatment of CKD and with worse glomerular filtration rate[9]. Thus, the use of NLR in HD patients seems to be more related to complications inherent to cardiovascular events and renal function than to sarcopenia parameters. As strengths of our study, the first work to evaluate the association of NLR with strength and muscle mass in HD patients. As limitations of the study, we present a small sample, we used BIA instead of DXA, and we cannot extrapolate the result to all individuals who have kidney disease.

CONCLUSION

NLR is not associated with muscle mass, strength, and functional capacity in HD patients.

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Conflict of interest: The authors declare that there are none.