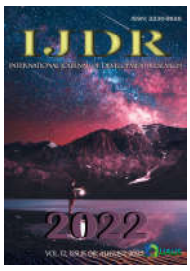
ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 12, Issue, 08, pp. 58097-58100, August, 2022
https://doi.org/10.37118/ijdr.25076.08.2022



RESEARCH ARTICLE OPEN ACCESS

RELATION BETWEEN FOREARM VASCULAR MORPHOFUNCTIONALITY OF HANDGRIP STRENGTH IN PATIENTS WITH STAGE 4 AND 5 CHRONIC KIDNEY DISEASE: A CROSS-SECTIONAL STUDY

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ARTICLE INFO

Article History:
Received 17th June, 2022
Received in revised form
23rd June, 2022
Accepted 08th July, 2022
Published online 22th August, 2022

Key Words:

Renal Insufficiency,
Arteriovenous Fistula,
Muscle strength, Renal dialysis.

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ABSTRACT

Objective: To evaluate the relation between handgrip strength and vascular characteristics of patients with stage IV and V chronic kidney disease (CKD) under conservative or dialysis treatment. **Method:** A cross-sectional study with 41 CKD patients in stages IV and V under conservative or dialysis treatment were recruited. Radial artery and cephalic vein diameters, mean radial flow velocity, arterial systolic peak and venous distensibility (ultrasonography), handgrip strength (dynamometry) and non-dominant upper limb forearm circumference (perimetry) were evaluated. **Results:** A relation between handgrip strength and radial artery diameter was observed at 10cm (R^2= 23.4%; β= 10.80; CI95%= 1.38-20.21; p= 0.02) and at 20cm (R^2= 21.3%; β=7.44; CI95%= 0.16- 14.72; p= 0.04), and with the distensibility at 20cm (R^2= 25.9%; β= 6.24; CI95%= 1.39-11.09; p= 0.01). **Conclusion:** There was a relation between handgrip strength and vascular diameters and venous distensibility in the proximal forearm segments.

Citation: ***Tatyane Gomes de Oliveira, Shirley Dias Bezerra, Juliana Rodrigues da Silva, Elaine Cristina Santa Cruz de Moura, Juliana Fernandes S. Barbosa, Patrícia Érika de Melo Marinho.*** "Relation between forearm vascular morphofunctionality of handgrip strength in patients with stage 4 and 5 chronic kidney disease: a cross-sectional study*", International Journal of Development Research*, 12, (08), 58097-58100.

INTRODUCTION

The irreversibility and chronicity of chronic kidney disease (CKD) requires renal replacement therapy (RRT). In this scenario, hemodialysis (HD) is the most common modality of choice despite the technological progress of transplants (Gjorgjievski, 2019). It is necessary to create a vascular access to perform HD, with the arteriovenous fistula (AVF) being considered as the best choice of access and its creation is the most frequent (Balamuthusamy, 2020). Efficacy in the creation and maintenance of AVF is surrounded by factors that range from the necessary vascular characteristics to the performance of exercises which favor its maturation for its successful use (Dageforde *et al*., 2015; Wilschut *et al*., 2018). It is common to perform manual compression exercises during the maturation period, in addition to concentric isometric and isotonic exercises, seeking that the shear between the muscles and the vessels promote structural changes which contribute to more effective maturation, with secondary strength gain (Barbosa *et al*., 2018; Kong *et al*., 2014). However, little is known about if vascular parameters such as diameters of radial artery and cephalic vein, radial flow velocity, arterial systolic peak and venous distensibility are related to handgrip strength in CKD patients. Therefore, the aim of this study was to evaluate the relation between handgrip strength and vascular characteristics of patients with stage IV and V CKD under conservative or dialysis treatment.

METHODS

Study Design: A cross-sectional study conducted from April 2018 to June 2019 with conservative treatment of stage 4 and 5 CKD patients followed up at a university hospital in Recife and patients with CKD under regular HD without AVF and using temporary venous access.

This study followed the norms of the Reporting of Observational Studies in Epidemiology - STROBE (Cuschieri, 2019). The study was approved by the Institutional Research Ethics Committee (2,532,265) in accordance with National Research Ethics Committee Resolution 466/2012 and is in accordance with the principles established by the Helsinki Declaration. The sample was obtained by convenience and consisted of 41 individuals selected during the study period.

Eligibility criteria: Patients with stage 4 and 5 CKD undergoing conservative treatment or HD, who had been using temporary venous access for up to 6 months, of both genders, aged between 30 and 70 years, with medical indication for the preparation of AVF. Those with a history of AVF in both upper limbs or who had undergone previous local vascular procedure or who performed manual activity with high loads were excluded.

Data collection: Data regarding age, gender, weight, and height were collected and the patients' body mass index (weight/height^2) was calculated, as well as the presence of comorbidities and CKD stage. Patients were evaluated for vessel morphology and performance, handgrip strength, and circumference of the arm eligible for AVF.

Vessel ultrasound: Non-invasive hemodynamic assessment of the forearm was performed by ultrasound [Sonoace R3 (Samsung Medison - South Korea)]. The diameters of the radial artery and the cephalic vein, the mean velocity (in cm/s) and the radial artery flow (systolic peak in cm/s), as well as the cephalic vein distensibility were analyzed. The patient remained seated with their elbow flexed at 45 ° and resting on the table during the evaluation, with the palmar face up. Three measurements were made at 2, 10 and 20cm of the forearm from the styloid process of the radius(Barbosa, 2018) and the highest value between the measurements was considered since they differed by less than 10%.

Handgrip strength : Hand grip strength (HGS) was performed on the non-dominant upper limb by manual dynamometry (Smedley Dynamometer - hand type, Saehan - Korea), with the patient sitting, shoulders in neutral position, elbow flexed at 90 º, forearm in neutral position and the wrist at 0 º to 15 º radial deviation. Three measurements were performed with a two-minute rest interval between them, and the highest value obtained from the difference between the measurements was less than 10% (KgF) (Kong *et al*., 2014). The predicted value for each patient was determined from prediction equations proposed by Novaes *et al*. (2009), to identify lower than expected values for men and women.

Forearm circumference: Forearm circumference was measured on the non-dominant limb with the patient remaining in the same position with a measuring tape (retractable measuring tape-Sun Special, Brazil) positioned two centimeters distal to the cubital fossa (Kong *et al*., 2014).

Statistical analysis: Descriptive data were presented in frequency distribution tables for categorical variables and central tendency and dispersion measures for numerical variables. The Kolmogorov-Smirnov test was used to verify the normality distribution and the Levene test for homogeneity of variances. The comparison of means was performed using the t-test for independent samples. Multiple linear regression was performed to analyze a possible influence of HGS on vascular variables. The relation between the handgrip strength and the representative variables of vascular morphofunctionality were analyzed separately in order to avoid multicollinearity between the variables, being adjusted for gender and age. Statistical analysis of the results was performed using the Statistical Package for Social Sciences (SPSS) version 20.0, with $p < 0.05$ and a confidence interval of 95% as significant.

RESULTS

A total of 21 of the 41 (51.2%) patients were under conservative CKD treatment and 20 (48.8%) underwent hemodialysis. Those who underwent HD had a mean RRT time of 3.5 ± 1.5 months. The characteristics of the patients who participated in the study are shown in Table 1. The sonographic, strength and forearm circumference characteristics are described in Table 2. According to the multiple linear regression, the HGS was related to the radial artery diameter at 10cm (R^2 = 23.4%; β= 10.80; CI95%= 1.38-20.21; p = 0.02) and at 20cm (R^2 = 21.3%; β= 7.44; CI95%= 0.16-14.72; p = 0.04), and with the distensibility at 20cm (R^2 = 25.9%; β= 6.24; CI95%= 1.39-11.09; p = 0.01) (Table 3).

Table 1. Sociodemographic and clinical characteristics of the patients included in the study

Variables	Conservative (n=21)	Hemodialysis (n=20)
	n (%) / Mean ± SD	n (%) / Mean ± SD
Gender		
Female	10 (47.6%)	12 (60%)
Male	11 (52.4%)	8 (40%)
Age (years)	57.52 ± 8.65	52.6 ± 7.32
BMI (Kg/m^2)	27.16 ± 2.87	25.67 ± 2.67
CKD stage		
4	10 (47.6%)	6 (30%)
5	11 (52.4%)	14 (70%)
Comorbidities		
SAH	7 (33.3%)	6 (30%)
DM	8 (38.1%)	8 (40%)
SAH+DM	6 (28.6%)	6 (30%)

Legend: SD: Standard Deviation; CKD: Chronic Kidney Disease; GFR: Glomerular Filtration Rate; SAH: Systemic Arterial Hypertension; DM: Diabetes Melittus.

DISCUSSION

Patients undergoing conservative treatment had similar vascular characteristics to those under dialysis treatment; however, the former had higher handgrip strength and forearm circumference. HGS was related to arterial and venous morphological characteristics in the proximal forearm segments.

Vascular morphological and functional characteristics: Both conservative and regular HD patients in our study had adequate arterial and venous diameters for creating the AVF. The observed values are in accordance with those suggested in the literature as being favorable to the success of creating adequate radial-cephalic distal access, with arterial and venous diameters greater than 1.5mm and 2mm, respectively (Dageforde *et al*., 2015; Nakata *et al*., 2016). However, other aspects need to be taken into account for successful access creation or maturation, such as age, the presence of peripheral vascular disease, diabetes mellitus, stenosis, thrombosis or calcification, which may imply in AFV failure (Han *et al*., 2016). The patients in our study had a high frequency of diabetes mellitus. Studies suggest that the presence of this disease reduces vascular adaptability in patients with CKD, interfering with the ability to create and maintain an AVF, as well as increasing primary failure and patency rates (Monroy-Cuadros *et al*., 2012; Nanani *et al*., 2019).Considering that diabetes mellitus is not solely responsible for maturation failure, (Allon *et al*., 2011; Sedlacek *et al*., 2001) monitoring the vascular condition by ultrasonography in these patients is necessary in order to monitor the possible changes along the course of the renal disease.

Handgrip strength: The patients in this study had preserved muscle strength compared to predicted, although loss of skeletal muscle loss with worsening renal function is expected, (Zhou *et al*., 2018) since the imbalance between synthesis and protein degradation, in addition to the presence of metabolic acidosis, nutritional deficiencies and chronic inflammation (Lee *et al*, 2021), play a role in protein catabolism (Thomas and Mitch, 2013; Wang and Mitch, 2014). Our findings conflict with the results presented by Lee *et al* (2021). They analyzed data from 18,756 Koreans derived from the Korea National Health and Nutrition Examination Survey (KNHANES) conducted from 2014 to 2017, which has shown that the CKD stage was associated with low HGS (Lee *et al*, 2021). Despite Lee *et al* (2021) presented results from an extensive national database, the values of

Table 2. Ultrasound characteristics of radial artery and cephalic vein, dynamometry and circumference of the study patient

Variables	Conservative (n=21)	Hemodialysis (n=20)	p-value*
	n (%) / Mean ± SD	n (%) / Mean ± SD	
Radial Artery (2cm)			
Diameter (mm)	2.48 ± 0.44	2.19 ± 0.25	0.016
SP velocity (cm/s)	28.94 ± 7.31	29.23 ± 2.05	0.863
Mean velocity (cm/s)	11.06 ± 6.93	16.49 ± 2.17	0.002
Radial Artery (10cm)			
Diameter (mm)	2.37 ± 0.27	2.25 ± 0.13	0.095
SP velocity (cm/s)	26.30 ± 6.43	29.65 ± 3.83	0.051
Mean velocity (cm/s)	11.47 ± 4.62	15.92 ± 2.18	0.0004
Radial Artery (20cm)			
Diameter (mm)	2.66 ± 0.32	2.56 ± 0.29	0.271
SP velocity (cm/s)	24.70 ± 7.58	27.20 ± 3.64	0.190
Mean velocity (cm/s)	10.22 ± 4.88	11.88 ± 1.44	0.150
Cephalic vein (2cm)			
Diameter (mm)	2.49 ± 0.38	2.40 ± 0.28	0.393
Distensibility (mm)	2.54 ± 0.43	2.19 ± 0.44	0.014
Cephalic vein (10cm)			
Diameter (mm)	2.39 ± 0.35	2.34 ± 0.15	0.521
Distensibility (mm)	2.44 ± 0.45	2.49 ± 0.40	0.690
Cephalic vein (20cm)			
Diameter (mm)	2.71 ± 0.40	2.64 ± 0.22	0.516
Distensibility (mm)	2.70 ± 0.48	2.40 ± 0.34	0.285
Dynamometry (KgF)	35.95 ± 8.62	31.10 ± 3.97	0.027
Forearm circumference (cm)	26.07 ± 2.43	23.92 ± 0.58	0.001

Legend: SD: Standard Deviation; SP: Systolic peak; * T-test for independent samples; $p < 0.05$.

Table 3. Relation between handgrip strength and radial artery and cephalic vein morphofunctionality

Vascular Morphofunctionality	Dynamometry				
	β	R^2	95%CI		p-value
RA Diameter (10cm)	10.80	23.4%	1.38	20.21	0.02
RA Diameter (20cm)	7.44	21.3%	0.16	14.72	0.04
SP Velocity (20cm)	0.30	18.6%	-0.05	0.67	0.09
Distensibility (20cm)	6.24	25.9%	1.39	11.09	0.01
Mean Velocity (20cm)	-0.38	16%	-0.98	0.21	0.20

Legend: RA: Radial Artery; SP: Systolic Peak; All variables were adjusted for gender and age.
* Multiple Linear Regression; $p < 0.05$.

HGS were within the normal range, with a small percentage of individuals presenting low values between CKD stages. The maintenance of HGS in our study requires an explanation. The association of this measure with the body composition assessment could better reflect the appendicular muscle mass condition (upper and lower limbs) as it is associated with its function (Carrero *et al*., 2016), however, it was not possible to perform it. Jiang *et al* (2020), demonstrated a stronger association between measurements of limb muscle mass and muscle strength in Asians, black and white CKD patients. According these authors, age, loss of appendicular muscle and body fat gain were associated with muscle weakness. Antoher study reported a weak association between muscle mass and HGS in patients receiving hemodialysis, and described that HGS were only modestly correlated with muscle mass (Kittiskulnam *et al*., 2017). Despite these conflicting results, more studies are necessary to investigate conservative stage and hemodialysis patients.

Relation between vascular morphofunctional characteristics and handgrip strength: The relation between handgrip strength, vascular diameters and distensibility was only observed in the 10 and 20cm segments of the forearm in the patients in our study. Strength preservation associated with greater muscle mass in this region may favor vascular adaptations, triggering vascular functional and structural changes, with increased compliance and distensibility of these vessels (Padilla *et al*., 2011). The implications of this relation for clinical practice seem to justify the importance of performing isometric and isotonic exercises for patients who will have an AVF performed in more proximal forearm regions, thus ensuring that the muscles of this segment can act to promote necessary changes for the vessels that will be used to make the fistula. Barbosa *et al* (2018), demonstrated that an 8-week program of concentric isometric and isotonic exercises in elbow and wrist flexors was sufficient to increase the diameters of the cephalic vein measured at 2 and 10 cm and of the radial artery at 2, 10 and 20 cm from the styloid process of the radius, in addition to also presenting an increase in HGS in patients with CKD before AVF creation.Similarly, Kumar *et al* (2010) also found an increase in the diameters of the vessels reported above after an exercise program which consisted of squeezing a tennis ball repeatedly for at least daily for 28 days in patients with CKD prior to the AVF (Kumar *et al*., 2010). Radiocephalic AVF's are more recommended because they are distal (Magalhães *et al*., 2020), although the preparation in more proximal regions of the forearm seems to be more advantageous because they have greater muscle mass. The increase in muscle mass that can result from a physical exercise program and its development is proportional to the increase in blood circulation and the prominence of the veins (Andrade *et al*., 2021).

Study limitations: Our study has some limitations which need to be taken into consideration. One of these concerns the knowledge about the previous physical activity level of the patients involved in the study and if they performed exercises for their upper limbs. Another aspect to consider is the fact that we did not evaluate patients at other stages of CKD, which would enable a comparison between the stage and the relationship between handgrip strength and forearm vessel behavior.

Final considerations: Our study found a relation between handgrip strength and vascular morphological characteristics in the proximal forearm segments of CKD patients in stages 4 and 5. These patients had preserved strength and adequate arterial and venous diameters according to the recommendations for creating vascular access.

Financing: The authors of this study did not receive financial support for this research, authorship or publication of this article.

Declaration of conflicting interests: The author(s) declare(s) that there is no conflict of interest.

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